One Man . . . and Medicine on Strike and Influenza: "Pity the Poor Pig." See page 37.

Medical Tribune and Medical News

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world news of medicine and its practice—fast, accurate, complete

Vol. 17, No. 22 — Wednesday, June 23, 1976

First Clinical Trials:

Laser Beam Swiftly Treats GI Bleeding

By Nathan Horwitz
Medical Tribune Staff

Mount Beach, Fla.—Bleeding lesions of the gastrointestinal tract have been successfully controlled in the first clinical trials of endoscopic laser photocoagulation, teams from the United States and Germany reported here.

The procedure has proved safe, swift and well-tolerated in preliminary studies of 14 patients who were treated for lesions in nearly every part of the GI tract, the American Society for Gastrointestinal Endoscopy was told by the research groups.

Cumulatively, more than 130 bleeding sites in a wide range of disorders have been controlled by endoscopic laser electrocoagulation, with no instances of peritonitis or perforation, the investigators reported. The lesions

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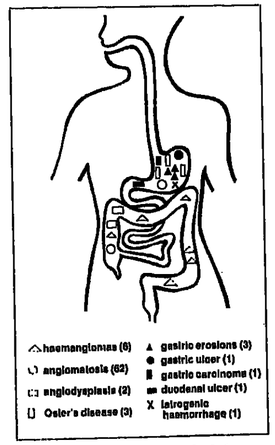


Gastrointestinal sites reached by endoscopic laser in first trials to control GI bleeding lesions are shown in drawing by German team. Group treated 80 lesions in 10 patients with wide range of disorders; U.S. teams treated 40 sites.

New Intensive Care Unit Protocol Avoids Quinlan-Type Dilemmas

Medical Tribune Report

Pittsburgh—A bold, new intensive care unit protocol designed to avoid Karen Quinlan-type dilemmas is now in place and working well at Presbyterian-University Hospital here, according to a physician who helped develop it.

"Along with guidelines previously established in 1969 for the determination of brain death, these new guidelines enable us to classify ICU patients into one of four categories: 'Total Support,' 'All But Cardiopulmonary Resuscitation (CPR),' 'No Extraordinary Measures,' and 'Brain Death,'" Dr. Michael Loughead told the International Congress on Emergency and Critical Care Medicine.

The protocol takes on special significance in light of surprising recent developments in the Quinlan case. After unexpectedly weaning Miss Quinlan from the respirator with at least temporary success, her physicians reportedly have resisted requests by the Quinlan family to cease feeding her high-calorie foods and refrain from giving her antibiotics. Foreseeing such eventualities, the Presbyterian-Hospital guidelines

Continued on page 16

Best Results Yet

Chemotherapy in Testes Ca Gives 89% Remissions

Medical Tribune World Service

Toronto—"The highest complete remission rate in any adult malignancy" has been achieved through the use of vigorous combination chemotherapy in patients with cancer of the testes, the leading cause of cancer deaths among men 25 to 34 years old, an Indianapolis physician told the meeting of the American Society of Clinical Oncologists.

Complete remissions were brought about in 16 out of 21 patients in a study group, all with advanced disseminated disease, reported Dr. Larry Einhorn, Associate Professor of Medicine at Indiana University Medical Center. Four of the patients achieved partial remissions, and reduced disease enabled two of these to undergo surgery to excise the remaining disease. One patient died of progressive tumor four days after treatment began. Seven additional patients, not included in the original study group, all achieved com-

Continued on page 27

Intermittent Heparin Effective, Convenient

Medical Tribune Report

New Orleans—Intermittent administration of heparin to patients with pulmonary embolism is more convenient, as less effective, and probably safer than giving the anticoagulant by continuous infusion, Dallas investigators have found.

The administration methods were compared for two groups of 18 patients each, assigned randomly to the route of therapy, in a study conducted by Drs. Lincoln J. Bynum and James E. Wilson, III, of the University of Texas Health Sciences Center at Dallas.

They reported the results of the trial here at the joint annual meetings of the American Lung Association, the American Thoracic Society, and the Congress of Lung Association Staff.

Recurrences of pulmonary embolism—three developed in patients on continuous heparin and two in patients treated intermittently—showed no statistically significant difference between the groups, according to the investigators.

They also found that the distribution of bleeding complications was roughly the same. Major bleeding occurred in three patients in each treatment group, and bleeding of lesser severity occurred

Continued on page 37

Six Liberty-Loving Physicians Among Those Who Signed the Declaration of Independence

Medical Tribune Report

Among the plotters at Philadelphia who signed the Declaration of Independence were six physicians. How many in the profession today would fix their names to a document of such radical intent? Few perhaps. Indeed, one recalls Harry Truman's observation, based on a poll taken in Madison, Wis., on July 4, 1951, that only a man on the street would endorse in writing the ideas contained in the Declaration.

As members of an economic elite, the six physicians and the 50 other signers could not have taken a step more at variance with their immediate self-interest. Almost none could have expected to prosper by a war and several came out poorer. "We mutually pledge to each other our Lives, our Fortunes and our sacred Honor," they declared. The vow was risky because had the war been lost, these men would have been considered defeated traitors rather than successful revolutionaries.

The best known today of the medical signers of the Declaration was Dr. Benjamin Rush (1746-1813) of Philadelphia. At the University of Edinburgh, he not only learned medicine but republican principles as well. Later setting in motion medical, political and social changes of lasting consequence, he established the first dispensary for the poor in the U.S., raised the study of mental illness to a scientific plane, championed higher education for women, and urged legal control of drinking. As a first-line physician, he reportedly saved no fewer than 6,000 people from death from yellow fever in the Philadelphia plague of 1793.


Dr. Bartlett


Dr. Hall


Dr. Rush


Dr. Thornton


Dr. Wolcott

Samuel Adams
Dr. Samuel Adams' Signature

Other medical signers were less prominent as physicians, but Dr. Josiah Bartlett (1729-1795) became governor of New Hampshire, Dr. Lyman Hall (1725-1790) governor of Georgia, and Dr. Oliver Wolcott (1726-1797) governor of Connecticut. Dr. Matthew Thornton (1714-1803) served as judge and legislator, and Dr. Samuel Adams (1745-1819), obscured in history by a more famous Adams to the extent that no portrait of him exists, wrote revealing diaries and finished his life as a country physician in Bath, Maine.

Progenital Disorders Confirmed in Sons of Diethylstilbestrol-Treated Women

Medical Tribune Report

LAS VEGAS—Two studies confirming and extending earlier observations of progenital disorders in men whose mothers were treated during pregnancy with diethylstilbestrol (DES) were reported here at the 71st annual meeting of the American Urological Association.

Dr. William G. Gill, Associate Professor of Urology at the University of Chicago, has found an increase both of epididymal cysts and of "severely pathological" semen in his DES-exposure group, compared to controls. And Dr. Alvin D. Cosgrove, Professor of Urology at the University of Southern California, has found a "significantly higher" incidence of urinary problems, male abnormalities, and other genitourinary abnormalities in a DES-exposed group, compared with controls.

Prompted by 1970 Report

Both studies were prompted by a 1970 report demonstrating a link between DES-exposure and vaginal cancer in adolescent girls. Neither Dr. Gill nor Dr. Cosgrove, however, said they could find cancerous changes in the young men they studied.

Approximately one million American men are believed to be potentially affected, Dr. Cosgrove said in an interview, adding that "they represent a finite group insofar as DES causes such side effects only in offspring." He declared that there is no justification for a "backlash" against use of the drug in other than pregnant women.

'Ready-Made' Population

Dr. Gill's study population was "ready-made," the Chicago investigator told MEDICAL TRIBUNE. A prospective study of the efficacy of DES was performed at Chicago's Lying-In Hospital 22 years ago, evaluating 840 women receiving DES and 806 receiving placebos. Dr. Gill and his coworkers were able to trace and evaluate 150 of the DES-exposed male offspring and 161 of the control group offspring. All were aged 21 to 23.

"Epididymal cysts, hypotrophic testes, and capsular induration of the testes were among the more common genital lesions found in more than 25% of 159 DES-exposed males as compared to a 6.5% incidence in 161 control males," Dr. Gill said.

Further, spermatozoa analyses revealed severely pathological changes, with an Eliasson score greater than 10, in 32% of 31 DES-exposed males and none of 20 control males. (The Eliasson score, Dr. Gill noted, is a sum of the scores for sperm count, % motility, motility grade, and morphology.) The abnormal physical findings combined with severe sperm abnormalities amounted to a 23% incidence in the DES-exposed males compared with 0% of the control males.

Cytologic examinations did not demonstrate malignant cells from urines, prostatic fluids, or cyst aspirates, Dr. Gill added. But, he said, "It is too early to determine definitively whether malignant lesions comparable to the vaginal and cervical clear-cell adenocarcinomas in DES-exposed female offspring will develop in the prenatally DES-exposed human males." Moreover, Dr. Gill said, "one needs to follow these and expanded numbers of patients carefully with regard to the probable association of DES-exposure and subnormal fertility."

Dr. Cosgrove sent questionnaires to 306 DES-treated mothers of male offspring, and to the mothers of 231 age-matched controls. Subsequently, 11 of the DES-exposed and 4 of the control sons were located and brought in for physical examination. "While three of the four control males were found to have no abnormality," Dr. Cosgrove said, "only two of the 11 DES-exposed were found to be urologically without blemish."

Dr. Cosgrove told MEDICAL TRIBUNE that he feels his report is still "tentative," because the numbers are small and the abnormalities he observed are common. But, he said, he believes larger studies should be done, and he wants physicians to be aware of the problem and to look at their patients carefully.

Silicone Prosthesis Repairs Diseased Trachea

Medical Tribune Report

LOS ANGELES—The "problem-free" reconstruction of the diseased or obstructed trachea using a silicone prosthesis has been achieved in nearly 50 patients by Drs. William E. Neville and Paul J. P. Bolanowski at Harrison S. Martland Hospital in Newark, New Jersey.

Most of the patients are still "alive and well" up to five years after the prostheses were sutured into the tracheobronchial tree, Dr. Neville told the 56th annual meeting of the American Association for Thoracic Surgery held here.

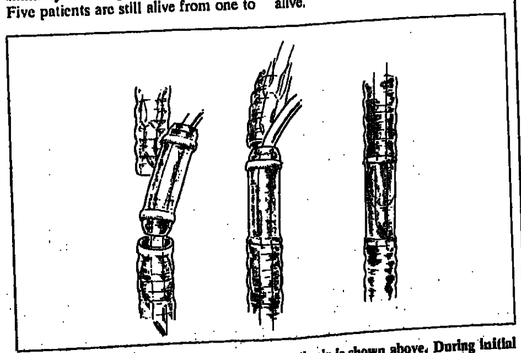
The prostheses, in either a straight tube or bifurcated form, were inserted in the tracheobronchial tree of patients whose airway was blocked or diseased to such an extent that it could no longer be reconstructed using the patient's own tissue, Dr. Neville said. The only complication (which could be corrected by fulguration) was the occurrence of granuloma near the point where the prosthesis was sutured to the tracheal tube, he explained.

"It is important to point out that graft disruption did not occur in any of the operations that we have reported and that in no case was infection a major complication. This is significant since it is frequently stated that one of the reasons that tracheal prostheses invariably fail is because a foreign body has been inserted into a contaminated area."

Over the past five years, following several years of experimentation with laboratory dogs, 18 patients had their tracheas reconstructed by Dr. Neville using the straight tubular graft. The prosthesis was sutured to the tracheal tube by means of a porous polyester fabric cuff surrounding the prosthesis itself, he said, explaining that 12 of the patients had a blocked trachea, four had adenocystic carcinoma and two had epidermoid carcinoma. Thirteen of the patients are still alive, while five others died from causes not related to the operation, including cardiac arrhythmia, drug overdose and progressive malignancies.

In eight other patients, the distal trachea and carina were replaced with a bifurcated graft and the results were similarly encouraging, Dr. Neville said. Five patients are still alive from one to five years after the operation, one patient died from preoperative lung abscesses and two died from disseminated cancer.

Dr. Neville said that the silicone prosthesis was the result of a search for a graft material that is air-tight, has a diameter consistency that is accepted by the host, causes a minimum of inflammation, is impervious to fibroblastic invasion, and that will be incorporated by the surrounding tissue. Since 1967, Dr. Neville has been installing the straight tube prosthesis, while in 1971 he was the first to install the bifurcated prosthesis. The patient who received that prosthesis is still alive.



Operative insertion of straight tracheal prosthesis is shown above. During initial anastomsis (left) patient is ventilated through distal trachea. Following completion of distal suture, endotracheal tube is withdrawn (center) and another inserted orally into graft for proximal anastomosis. Graft in place, at right.

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CLINICAL NEWS NOTE: *"Our results showed that extracts of breast cancer tissue markedly inhibited the stimulation of DNA synthesis by PHA [phytohemagglutin]. The data suggested that transcortin is not present within normal breast cancer cells, is synthesized and secreted by breast cancer cells, and that it protects the cancer cell from immunological attack by T-lymphocytes."* (Dr. Seymour Werthamer. See page 5.)

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EDITORIAL CAPSULES

. . . brief summaries of editorials or comments in current medical and scientific journals.

Telephone Diagnosis

". . . Reportedly, one-eighth of a pediatrician's time is spent on the telephone. Since these contacts often determine which patients need to be seen, it is vital that pediatricians obtain adequate telephone histories.

"The spouses of three house officers were trained to give simulated case histories for the following four common clinical situations: a five-year-old boy with a cough, a four-month-old girl with diarrhea, an 18-month-old boy with a rash, and a two and one-half year-old girl with vomiting.

". . . On contact with the pediatrician, the caller volunteered the child's age, sex, and chief complaint. Thereafter, additional information was given only in response to questions.

". . . Although most of the pediatricians in this study attempted to determine if an emergency existed, the histories obtained were often unexpectedly deficient. Only three of the ten pediatricians inquired if the five-year-old child with a cough had difficulty in breathing, which might signal pneumonia or epiglottitis. No pediatrician in practice more than five years asked questions about the hydration of the infant with diarrhea. In assessing rash, three of the ten pediatricians made no inquiries about the character of the eruption, leaving unanswered the question of potentially lethal purpuric illness. When presented with the complaint of vomiting, seven of ten physicians failed to ask about the presence of abdominal pain, thereby possibly overlooking the possibility of immediate surgery.

"Questions useful in diagnosis, prognosis, and initiating therapy were also often omitted. In inquiring about cough, no pediatrician asked about a history of allergy even though the calls were made at the peak of the pollen season. In assessing rash, only three out of ten physicians inquired about exposures to communicable diseases.

"Pediatricians with less than five years in practice answered the telephone more promptly, asked more questions, were more likely to ask questions relevant to life-threatening disease, and spent more time on the telephone than their more seasoned colleagues. Factors such as clinical insecurity, need for patients, and past experience perhaps affect such behavior as much as pediatric training programs do. . . ." *(Lawrence Greitzer, M.D., et al, J. Pediat, 88:880, May, 1976)*

Life-Death Decisions

Medical Tribune Report

BOSTON—There will be a Medical Symposium on Life-Death Decisions in Medicine sponsored by the National Right to Life Committee. This Symposium will be held at the Museum of Science, Boston, Mass., on Saturday, June 26, 1976. The guest luncheon speaker will be Sir A. W. Liley, perinatologist, from Auckland, New Zealand.

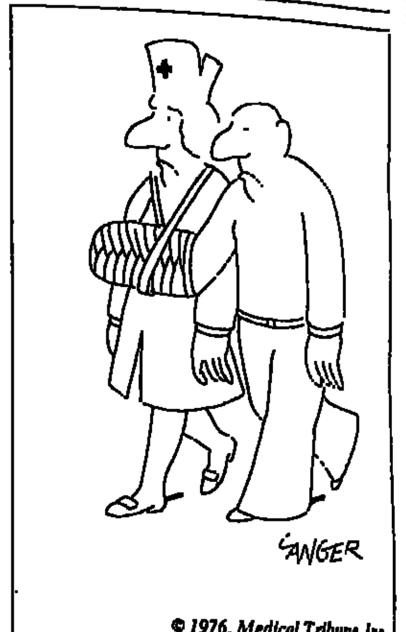
NEI To Evaluate Vitrectomy In Diabetic Retinopathy

Medical Tribune Staff

RESTON, VA.—The National Eye Institute has launched a major, long-term study to compare the relative risks and benefits of early and late vitrectomy in the management of diabetic retinopathy.

Announcing the study at a seminar sponsored by Research to Prevent Blindness, Inc., NEI Associate Director, William F. Raub, Ph.D., said the usual practice is to wait for a year after the occurrence of severe vitreous hemorrhage before performing vitrectomy. However, the rapid, substantial improvement in visual acuity that follows vitrectomy in many instances has led to a feeling on the part of some ophthalmologists that the procedure might be undertaken safely without waiting a year for the hemorrhage to clear on its own. It is hoped that the Diabetic Retinopathy Vitrectomy Study will provide information about the optimal time for performing the surgery.

Another aim of the study, according to Dr. Matthew D. Davis, Professor and Chairman of the Department of Ophthalmology, University of Wisconsin Medical School, is to "evaluate early vitrectomy in a carefully controlled setting *before* it gains widespread use on the basis of uncontrolled reports."



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Protein Found in Breast Ca May Block Immune System

By JOHN HENAHAN
Special Tribune Correspondent

ANAHEIM, CALIF.—A protein found in human breast cancer tissue and not in normal breast tissue appears to shut down a major portion of the body's immune defense system, according to a paper presented here at the 60th annual meeting of the Federation of American Societies for Experimental Biology.

Called transcortin, the protein seems to interfere with the ability of T-lymphocytes to synthesize DNA and reproduce themselves, said Dr. Seymour Werthamer of the pathology department of Methodist Hospital, Brooklyn, N. Y. He and Dr. Leonard Amaral isolated and purified transcortin from human breast cancer for the first time about a year ago, but were unable to find it in normal tissue.

To prove that the transcortin reacted specifically to shut down the T-lymphocytes, Drs. Werthamer and Amaral incubated transcortin from breast cancer tissue with phytohemagglutin (PHA). The substance usually acts to incite DNA production in T-lymphocytes.

"Our results showed that extracts of breast cancer tissue markedly inhibited the stimulation of DNA synthesis by PHA," Dr. Werthamer said. "The data suggested that transcortin is not present within normal breast cancer cells, is synthesized and secreted by breast cancer cells and that it protects the cancer cell from immunological attack by T-lymphocytes."

The Brooklyn researchers began looking for transcortin in breast cancer tissue after it was discovered that the placenta of the fetus produces the protein, which then migrates to the maternal sinus. They speculated at the time that the "presence of high levels of transcortin bathing the placental unit would protect the placenta from being attacked by the mother's T-lymphocytes and consequently the rejection of the fetus is prevented."

Other studies indicated that proteins which are found in embryonic tissue are frequently found in cancer tissue of the same type but not in related normal tissue. For example, a fetoprotein found in the embryonic liver is not found in the adult organ, unless it is cancerous. Those observations "caused us to examine breast cancer tissue for the presence of transcortin, since normal breast tissue is not known to synthesize this protein," Dr. Werthamer said.

He noted that the National Cancer Institute is now evaluating the transcortin findings as the basis for a potential diagnostic test for early breast cancer. Beyond that, he believes that the discovery could provide a biological approach to correcting the defect in the immune system which allows a breast tumor to grow and proliferate.

Stress Pioneer and Behavioral Biologist Win Kittay Awards

Medical Tribune Report

NEW YORK—A pioneer in the field of stress, Dr. Hans Selye, and a behavioral biologist who has added "a new dimension to the understanding of human motivation", James Old, Ph.D., were named the recipients of this year's $25,000 International Kittay Award, the world's largest prize in psychiatry.

Dr. Selye discovered the neuroendocrine basis of the stress syndrome, which, according to the New York-based Kittay Scientific Foundation, "gave to psychosomatic medicine a new model, not only for the development of illness, but for its treatment as well."

Dr. Selye, who is director of the Institute of Experimental Medicine and Surgery, University of Montreal, visualized the syndrome as a "call to arms" of the body's defenses and therefore designated it as the "alarm reaction." Since no animal can be maintained continuously in a state of alarm upon exposure to a stressor, adaptation or resistance ensues. After prolonged exposure, "adaptation energy" is depleted and exhaustion takes over, he hypothesized. The Canadian's research has contributed to the understanding of ulcers and other psychosomatic conditions.

Dr. Olds, Bing Professor of Behavioral Biology at the California Institute of Technology, discovered the area of the brain responsible for the reward-pleasure mechanism. His research has implications for anedonia of schizophrenia and "introduces a new dimension for the study of purposive behavior, as related to the need for a status of pleasure, independent of the gratification of a basic drive." His latest work on brain amines further clarifies learning and behavioral processes.

Don't Miss
THE GOOD DRUGS DO
Edited by the famous clinical pharmacologist, Dr. Lasagna, designed to be removed from Medical Tribune for your waiting room, it begins on Page 17.
FOR YOUR PATIENTS

IN CONSULTATION

What's New and Important About Cancer of the Prostate?

The Consultant

WILLIAM D. DEWYS, M.D.
Associate Professor of Medicine
Department of Medicine, Oncology Section
Northwestern University Medical School
Chicago, Ill.

PROSTATIC CANCER is the second leading cause of cancer deaths in males, and a number of recent developments point to the prospect of improved detection and care of patients with this disease. Improved assays of serum acid phosphatase and application of the carcinoembryonic antigen test have been evaluated for early detection of prostatic cancer, but neither of these assays is positive in enough early cases to be useful for early detection. Study for lactic dehydrogenase isoenzymes in expressed prostatic fluid may prove useful for early detection and Grayhack has found that the ratio LDH5/LDH1 is greater than 3 in 80% of patients with prostatic cancer, compared with 14% of patients with benign prostatic hyperplasia and 0% of normal persons.

Since optimum selection of treatment must be based on proper staging of the patient's cancer, there is increasing attention to proper application of staging evaluation. Measurement of prostatic acid phosphatase in bone marrow aspirates may increase the sensitivity of detection of bone marrow metastases over that obtained with morphologic studies of bone marrow aspirates or bone scan, so that patients with disease extending to the bone marrow may receive systemic therapy rather than local therapy. Also of value in staging is the lymphangiogram, which has been found to have a greater than 90% accuracy in evaluating lymph nodal spread from prostatic cancer. This information may also assist in proper planning of treatment.

A recent development which may have usefulness in selecting treatment for patients with prostatic cancer is the assay of cancer tissue for hormone-binding proteins. It is well known that the presence of hormone-binding proteins in breast cancer may predict for response to hormone manipulation, and it is hoped that assay of androgen-binding protein in prostatic cancer may predict for response to orchiectomy or estrogen therapy in patients with prostatic cancer. Positive results have been obtained in an animal tumor system, and human studies are currently in progress.

What tests are available for early detection of prostatic cancer?

The mainstay in the early detection of prostatic cancer is the rectal examination, which should be part of the annual physical examination of every male over age 40. The assay of isoenzymes of lactic dehydrogenase in prostatic fluid, mentioned above, may become more widely available and may prove of value in the early detection of prostatic cancer. In many patients early prostatic cancer does not have symptoms and the patient will not seek medical attention until he has symptoms referrable to metastatic disease. Development of pain referrable to bones or joints, especially in the back and pelvis region, in any male over age 50 should raise the question of metastatic cancer. In evaluating possible bony metastases, it is clear that a bone scan is more sensitive than bone X-rays, and a bone marrow biopsy and bone marrow aspirate for acid phosphatase are more sensitive than a bone scan.

What are the recommended treatments of choice for early prostatic cancer?

Patients with stage A cancer (no physical findings, but prostatic cancer discovered incidentally on histologic examination of resected prostatic tissue). Transurethral resection of the prostate may be considered adequate treatment in the majority of the cases. However, within the group of patients with stage A, some patients will develop recurrent disease which may be progressive, and these will generally be the patients who have undifferentiated tumors at histologic study. Therefore stage A patients with the poorly-differentiated tumors should be considered for radiation therapy to the prostatic area. For patients with stage B (a palpable nodule in the prostate, but no evidence of extension beyond the prostate) either a radical surgical prostatectomy or radical radiation therapy are worthwhile treatments and it is not clear which of these is better. If patients are good surgical risks, we would recommend surgical excision. If patients are not good surgical candidates, radical radiation therapy (7,000 R to the prostate) may be curative, but the morbidity of this dose of radiation may be significant. For patients with stage C disease (local extension outside of the prostate, but no evidence of distant metastases), radical radiation therapy probably is the treatment of choice.

What role does immunotherapy play in the treatment of prostatic cancer?

With the present state of the art of cancer immunotherapy, immunotherapy plays no role in the treatment of prostatic cancer. Active immunotherapy of a non-specific type, by injecting Bacillus Calmette-Guerin vaccine directly into the prostate has been studied and the results have been generally negative. Specific immunotherapy (tumor cell vaccine) has not been evaluated.

What is the recommended treatment for advanced prostatic cancer?

For the majority of patients with advanced disease (metastases) the recommended initial treatment is hormonal manipulation with the expectation that approximately 80% of the patients will experience subjective and/or objective improvement. Exceptions to this generalization are that patients with diffuse lung metastases or with liver metastases may not respond well to hormone manipulation and should be considered for chemotherapy. The choice of hormonal manipulation is either orchiectomy or estrogen therapy, and in the application of estrogen therapy it is now established that 1 mg of diethylstilbesterol is as effective as larger doses and is accompanied by less cardiovascular morbidity and mortality. If the patient fails to respond to an initial hormone treatment, the patient should be considered for chemotherapy. If the patient responds to initial hormone therapy and then subsequently relapses, alternate hormone therapy may be of value, but the response rate will be less than that to initial hormone therapy. By alternate hormone therapy we mean that if a patient has responded to orchiectomy he be considered for estrogen therapy and vice versa. Other hormone manipulations such as hypophysectomy or adrenalectomy have been evaluated but, in our opinion, the percent of patients responding and the duration of response are not sufficient to warrant the morbidity of these procedures.

For patients who fail to respond to hormone therapy or who are in relapse after hormone therapy, chemotherapy should be considered. The results of the National Prostate Cancer Project support the use of 5-fluorouracil or cyclophosphamide with both objective and subjective responses being better than that of patients receiving standard treatment (radiation therapy, analgesics, etc.). The studies of the Eastern Cooperative Oncology Group also support the value of 5-fluorouracil. Studies by the Southwest Oncology Group and the Eastern Oncology Group have also observed favorable responses to adriamycin, but this drug may have greater toxicity than either 5-fluorouracil or cyclophosphamide.

And finally, in the treatment of patients with advanced disease, symptomatic measures such as radiation therapy for painful bony metastases, use of a back brace to limit mobility in the region of painful metastases, use of adequate doses of analgesics, and other measures of supportive care may be of considerable symptomatic benefit to the patients.

Next In Consultation

DR. CLAUDE A. FRAZIER, of Asheville, N.C., author of *Insect Allergy: Allergic and Toxic Reaction to Insects and Other Arthropods*, will answer questions on what's new and important in the treatment of insect bites, the question of changing state laws to permit the sale of insect sting kits without prescription, and how to treat insect stings through hyposensitization carried out over a period of weeks.

Ear Tissue Study

Micro-thin slices of inner-ear tissue are positioned for electronmicroscope viewing by Dr. V. Terrance Rhodes, University of Minnesota. The school's study of hearing disorders comprises 18 projects, including human and animal work and effects of drugs and noise.

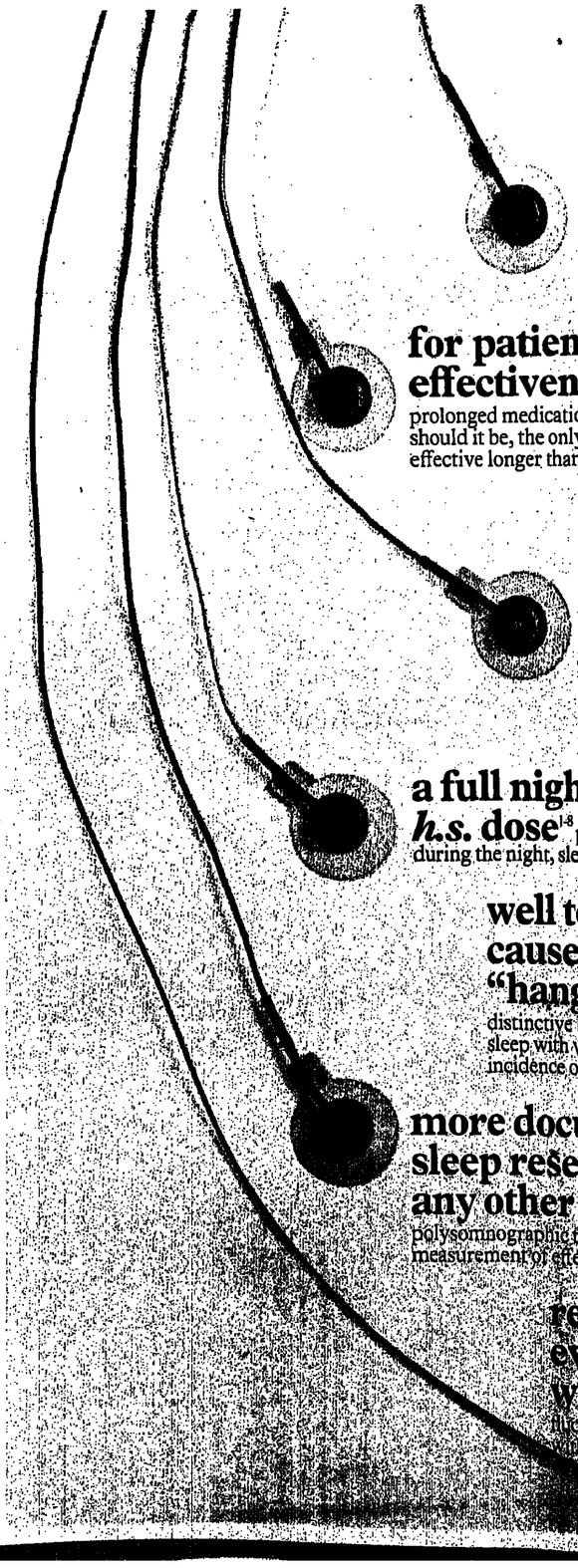
Faulty Respiratory Control, O_2 Lack Implicated in Sudden Infant Deaths

Medical Tribune Report

HERSHEY, PA.—Evidence suggesting that faulty respiratory control mechanisms and chronic lack of oxygen may play key roles in the etiology of sudden infant death syndrome (SIDS) has been found in two separate but related autopsy studies, according to a research team headed by Dr. Richard Maeye, Professor and Chairman of the Department of Pathology, Milton S. Hershey Medical Center here.

In one study, 85% of 56 SIDS victims showed abnormalities in their carotid bodies, the organs in the aorta that sense fluctuations in oxygen in the blood; 63% had fewer cells in their carotid bodies than controls and 23% had more. "... the finding of both hyperplastic and hypoplastic carotid bodies ... increases the possibility that diverse mechanisms are involved in their deaths, even if apneic episodes remain a common pathway," the investigators said in *Science* (191:567).

In the related study, Drs. Naeye, Philip Whalen, Monique Ryser, and Russell Fisher reported (*Am. J. Path.* 82:1) that about half of 85 SIDS victims had greater heart weights—a sign of chronic hypoventilation and hypoxemia—than controls. In addition, there were signs of chronic oxygen deficiency at the tissue level: increased muscle tissue in pulmonary arteries, increased volume of the chromaffin cells of the adrenal medulla that secrete stress hormones, abnormal retention of brown fat cells about the adrenals, abnormal growth of brainstem glial fibers, and abnormal retention of red blood cell production in the liver.



on average, sleep within 17 minutes that lasts for 7 to 8 hours with fewer nighttime awakenings[1] proved in patients with insomnia in 8 sleep research laboratory studies

for patients who need it, continued effectiveness over 28 nights[2,3]

prolonged medication for insomnia is generally not necessary; should it be, the only available sleep agent proved objectively to be effective longer than two weeks is Dalmane (flurazepam HCl)

proven effectiveness in elderly patients with verified insomnia[4]

the greater the degree of insomnia, the greater the objective improvement with Dalmane 15 mg administered for 7 nights *h.s.*—15 mg is the recommended initial dosage for elderly and debilitated to help preclude oversedation, dizziness or ataxia

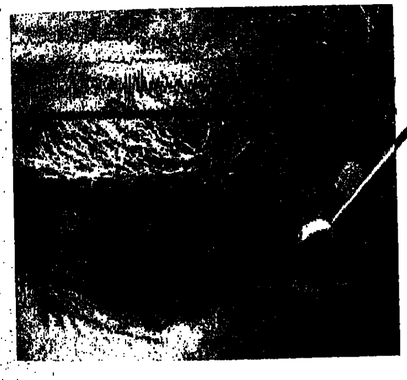
a full night's sleep with a single *h.s.* dose[1-8] patients fall asleep faster, awaken less often during the night, sleep longer without repeating dosage

well tolerated, seldom causes morning "hang-over"[1] Dalmane is a distinctive benzodiazepine specifically indicated for sleep with well-documented safety and low incidence of morning "hang-over"

more documentation from the sleep research laboratory than any other agent for insomnia[1-8]

polysomnographic techniques provide the most objective measurement of effectiveness possible

relative safety extending even to patients on chronic warfarin therapy[1,9] no unacceptable fluctuation in prothrombin time has been reported with Dalmane



The Dalmane® (flurazepam HCl) difference.

ROCHE

Please see following page for a summary of product information.

The Only Independent Weekly Medical Newspaper in the U.S.

Medical Tribune
and **Medical News**
Published by Medical Tribune, Inc.

Merits of the Past

THE MOST RECENT BOOK of the noted child psychologist, Bruno Bettelheim, Ph.D., is one bearing the title, *The Uses of Enchantment: The Meaning and Importance of Fairy Tales*. In it Dr. Bettelheim presents the view that the fairy tales of the past were—and are—of great value in the developmental stages of childhood. Progressive educators, however, saw them as filled with malign influences, horrid and evil events, removed from the realities of existence. Fairy tales fell out of favor and were replaced by such "good" reading as *The Little Engine That Could*.

The reviewer of the book in the *New York Times* described Dr. Bettelheim's prose as "dry and theoretical," but soon found himself persuaded by the merit of his thesis. Dr. Bettelheim convincingly demonstrates that fairy tales provided the catharsis for children that Greek drama sought to provide for adults—a purification of the emotions through art, as the dictionary puts it. Fairy tales are not removed from the realities of existence but instead deal with all sorts of anxieties and fears that normally confront children—and provide symbolic and, sometimes, protective resolutions for them. Dr. Bettelheim hopes that "a proper understanding of the unique merits of fairy tales will induce parents and teachers to assign them once again to that central role in the life of the child they held for centuries."

Meanwhile, a book published in England, *Teaching Styles and Pupil Progress*, reports the results of a four-year study in educational research under the direction of Neville Bennett, Ph.D., comparing the progress of pupils taught by traditional and progressive educational methods over a four-year program. In any given year, the pupils taught by progressive methods lagged by three to five months over those taught by traditional methods. A comment in *New Scientist* that bears repetition notes that "the tone adopted by Dr. Bennett and his colleagues is that unstructured learning places too much responsibility on the necessarily immature shoulders of young school children. What they need is a structured framework which guides disciplined progress while leaving scope for creativity. Progressive 'finding-out' methods may well lead to nothing more substantial than day dreams and sky gazing."

An irresistible question comes to mind now that merit is found both in fairy tales and structured traditional learning for children. What about some of the adult innovations, such as the changes in medical education and, particularly, in the responsibility placed on the house staff of our more advanced medical institutions? Diagnostic studies and medication orders in these centers can be written only by the house staff and the attendings may or may not be listened to. Perhaps the more structured techniques of past medical education of the house staff had unperceived merit. What is more, perhaps they led to more economical use of diagnosis and therapy.

A Curious Footnote

THE ASSOCIATION OF AMERICAN TRIAL LAWYERS sought to bar the Medical Society of the State of New York from what it was pleased to call "false advertising" in regard to medical malpractice legislation pending in that state. In its efforts to do so, the Association turned to the Federal Trade Commission.

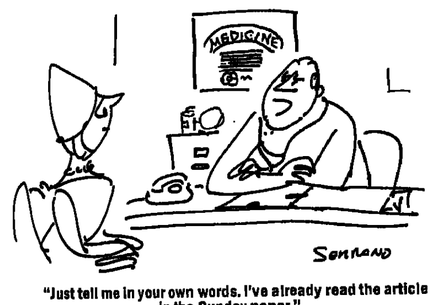
The Medical Society had made use of a 12-page advertising supplement that appeared in seven New York State newspapers during the month of April. The supplement cited the reasons why the Society, because of the extraordinary increase in the cost of malpractice insurance, favored pending legislation that places a ceiling on contingency fees lawyers may receive and limits the money a plaintiff may obtain in damages for "pain and suffering."

According to the Association's petition to the FTC, the Society's advertisement was criticizable for calling the McGill Commission "impartial." The Commission, which was appointed by Governor Carey to study and make recommendations on medical malpractice legislation, was not impartial by the Association's standards "since five of the nine members of the Commission were at one time or another connected directly or indirectly with the medical profession and the providers of health care."

A curious footnote to all this is that a member of the board of governors of the Association of American Trial Lawyers denied at a press conference that trial lawyers were upset because the legislation was a threat to a prime source of their income.

On Laser Photocoagulation

CLINICAL QUOTE: *"This form of therapy has the potential of converting emergency surgery for acute upper GI bleeding into a relatively elective procedure and may offer an alternative mode of therapy for lesions not readily amenable to surgery."* (Dr. Richard M. Dwyer, University of Southern California, at the American Society for Gastrointestinal Endoscopy. See p. 1.)



"Just tell me in your own words. I've already read the article in the Sunday paper."

LETTERS TO TRIBUNE

'Family Ganging,' Etc.

I was amused and at the same time distressed by your dictionary in the *Book Biopsy* column (MT, April 28).

"Family ganging": This definition [seeing a whole family at the same time] indicates that family ganging is iatrogenic and seen only in the so-called mills. This is, of course, inaccurate in that in my practice the family ganging is a family-induced factor in which the medicaid recipients do frequently totally disrupt my appointment-drop-in system by descending upon me en masse. I can understand that frequently several members of the family are ill with contagious disease and need to be treated, but feel that since the service is provided free that it is used in many cases where it would not be used if the patient or patients were paying for it. A similar abuse exists in regard to unnecessary use of the emergency room after office hours as a mere convenience to the patient and an inconvenience to the physician.

I was also amused at the terminology and definitions kind of scattered about the article.

"Skimming": I recall as a Mafia or gangster term applied to removing the best part of financial intake or profit or to anything else and in comparing the action to the dairy process of removing the cream from the rest of the milk.

I congratulate you on your column and feel that distortions in it which may reflect unfavorably upon physicians are motivated by our federal bureaucracy's effort to expand themselves and their like by casting uncomplimentary suggestions upon others.

Perhaps this is an ego trip for those bureaucrats and that they are aware both morally and in all other respects that they are inferior to the medical professions and would like to make themselves and others feel the reverse is true.

GEORGE W. FORT, M.D.
Abbeville, N.C.

Horsemen of Death

Dr. Pfeiffer chides Dr. Sackler for not citing statistics on firearm deaths, and says that the number "is really only a pitifully few." On the contrary, firearms are second only to the automobile as a source of fatal injury: the annual number of deaths in the U.S. from gunshot wounds is over 28,000.

About half of these deaths are homicides: generally the trigger is pulled by someone known to the deceased, someone without a criminal record. In over 11,000 homicides in 1974, the weapon was a handgun. Easily concealed, too readily available, the handgun often replaces the less lethal knife, thus changing many a victim's destination from emergency room to morgue.

Some 12,000 suicides each year involve firearms. And even accidental gun deaths—some 2,500 each year—are "pitifully" many, rather than few. All too often, weapons intended for protection are accomplishing just the opposite.

Alcohol, tobacco, and firearms. Yes, these three "Horsemen of Death" should be considered together—not only because of their tremendous impact on health, but also because they all come under the jurisdiction of the same non-health agency.

SUSAN P. BAKER, M.P.H.
Associate Professor
Johns Hopkins University
School of Hygiene and Public Health
Baltimore, Md.

The Good Drugs Do

I was most impressed with the recent insert, "Fighting Rheumatoid Arthritis" (MT, May 12).

I think this would be a marvelous piece of literature to distribute to some of our patients.

ARNOLD BLACK, M.D.
Chicago, Ill.

PATIENT EDUCATION can begin in your waiting room if you'll remove the special section from this paper titled **THE GOOD DRUGS DO** and put it in your waiting room. Edited by the top pharmacologist, Dr. Louis Lasagna, it will help build doctor-patient relationships. **It begins on Page 17**

Ismelin® sulfate
(guanethidine sulfate)

Esimil®

guanethidine monosulfate	10 mg
hydrochlorothiazide	25 mg

> **WARNING**
> This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

INDICATIONS
Ismelin
Moderate and severe hypertension either alone or as an adjunct.
Esimil
Hypertension. (See box warning above.)
CONTRAINDICATIONS
Guanethidine: Known or suspected pheochromocytoma; hypersensitivity; frank congestive heart failure not due to hypertension; use of MAO inhibitors.
Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.
WARNINGS
Antihypertensives are potent drugs and can lead to disturbing and serious clinical problems. Physicians should be familiar with all drugs and their combinations before prescribing, and patients should be warned not to deviate from instructions.
Guanethidine

> Warn patients about the potential hazard of orthostatic hypotension, which can occur frequently and is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. To help prevent fainting, warn patients to sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during the initial period of dosage adjustment and with postural changes. The potential occurrence of these symptoms may require alteration of previous daily activity. Caution patients to avoid sudden or prolonged standing or exercise while taking the drug.

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression.
If possible, withdraw therapy 2 weeks prior to surgery to reduce the possibility of vascular collapse and cardiac arrest during anesthesia. If emergency surgery is indicated, administer preanesthetic and anesthetic agents cautiously in reduced dosage and have oxygen, atropine, vasopressors, and IV solutions ready for immediate use to treat vascular collapse. Vasopressors should be used with extreme caution in patients on guanethidine because of the possibility of augmented response and the greater propensity for cardiac arrhythmias.
Dosage requirements may be reduced in presence of fever. Exercise special care when treating patients with a history of bronchial asthma, since their condition may be aggravated.
Hydrochlorothiazide
Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.
Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.
Thiazides may be additive or potentiative *of the action of other antihypertensive drugs.* Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.
Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma.
The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.
Usage in Pregnancy
Guanethidine: The safety of guanethidine for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.
Hydrochlorothiazide: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.
Nursing Mothers
Thiazides cross the placental barrier and appear in cord blood and breast milk.
PRECAUTIONS
Guanethidine: The effects of guanethidine are cumulative over long periods; initial doses should be small and increased gradually in small increments. Use very cautiously in hypertensives with: renal disease and nitrogen retention or rising BUN levels; coronary disease with insufficiency or recent myocardial infarction; cerebral vascular disease, especially with encephalopathy. Do not give guanethidine to patients with severe cardiac failure except with extreme caution.

In incipient cardiac decompensation weight gain or edema may be averted by the administration of a thiazide. Remember that both digitalis and guanethidine slow the heart rate. Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone.

Amphetamine-like compounds, stimulants (eg, ephedrine, methylphenidate), tricyclic antidepressants (eg, amitriptyline, imipramine, desipramine) and other psychopharmacologic agents (eg, phenothiazines and related compounds), and oral contraceptives may reduce the hypotensive effect of guanethidine. Discontinue MAO inhibitors for at least one week before starting guanethidine.

Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.

Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH.

Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

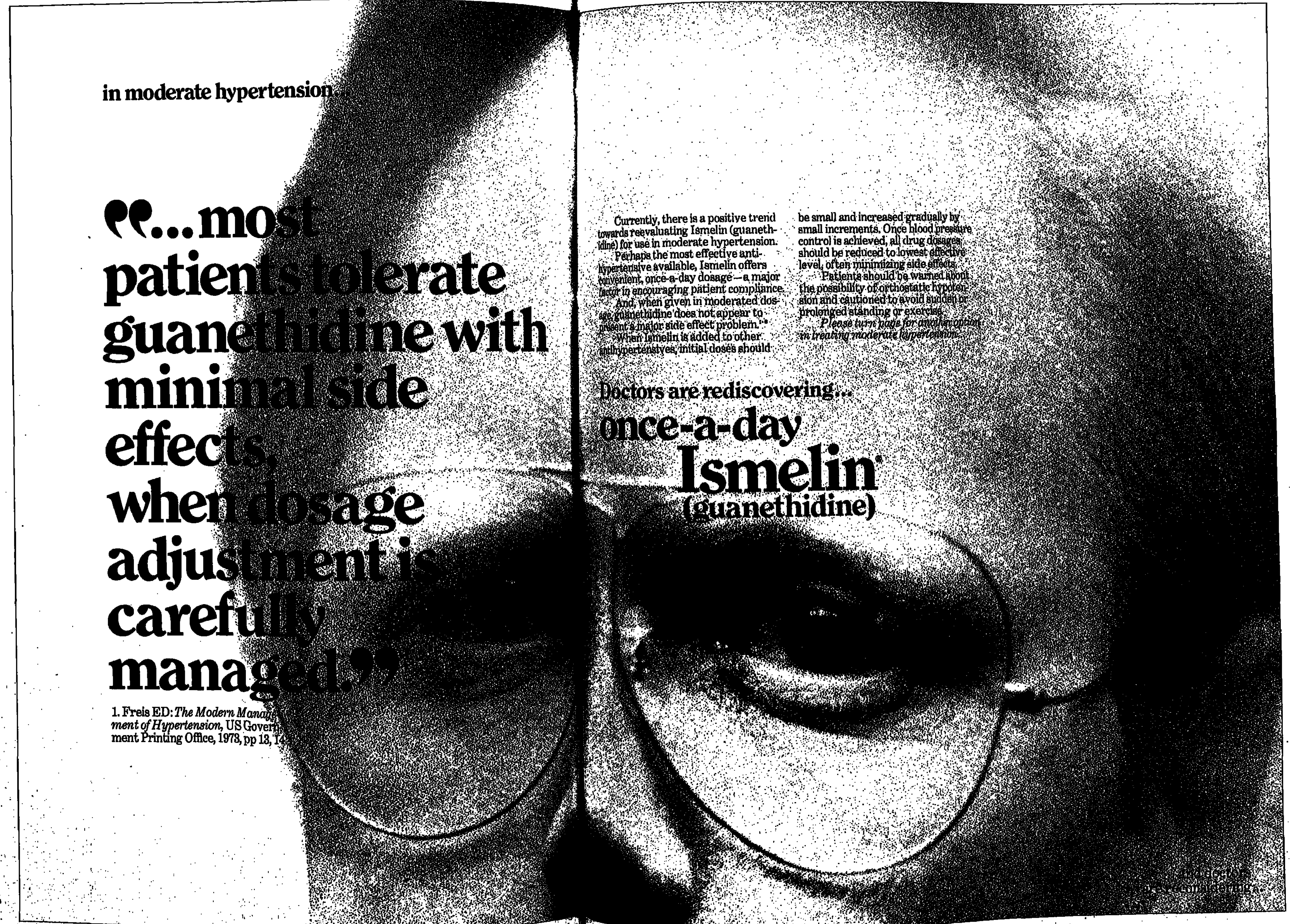
Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.

Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.

Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.
Thiazides may decrease serum PBI levels without signs of thyroid disturbance.
ADVERSE REACTIONS
Guanethidine: *Frequent reactions due to sympathetic blockade*—dizziness, weakness, lassitude, syncope. *Frequent reactions due to unopposed parasympathetic activity*—bradycardia, increase in bowel movements, diarrhea (may be severe and necessitate discontinuance of the drug). *Other common reactions*—inhibition of ejaculation, fluid retention, edema, congestive heart failure. *Other less common reactions*—dyspnea, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, ptosis of the lids, blurring of vision, parotid tenderness, myalgia, muscle tremor, mental depression, chest pains (angina), chest paresthesias, nasal congestion, weight gain, and asthma in susceptible individuals. Although a causal relationship has not been established, a few instances of anemia, thrombocytopenia and leukopenia have been reported.
Hydrochlorothiazide: *Gastrointestinal*—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis. *Central Nervous System*—dizziness, vertigo.

(Brief prescribing information continued on next page)



CIBA

Genetic Factors Help Identify Suicide Risks

Medical Tribune Report

NEW YORK—The evidence for genetic factors in suicide is now firmly enough based that "we can identify a group of individuals who are at special risk," a University of Iowa investigator declared here.

Dr. Ming T. Tsuang, Professor of Psychiatry, said this group is made up of persons with manic-depression, schizophrenia, or alcoholism who, in addition, also have a family history of suicide. Such individuals, he cautioned, "should receive special attention with regard to suicide-prevention measures."

Studies of twins have helped establish a genetic component in self-destruction, Dr. Tsuang told a seminar for science writers on "A Biological View of Suicide," sponsored by the Society to Conquer Mental Illness.

Citing a comprehensive review of twin data published in 1967, the psychiatrist noted that it had included pooled figures for 149 sets of twins of whom at least one member had committed suicide. In nine cases, the co-twin had also committed suicide, he said, and all nine instances were observed in monozygotic pairs.

The concordance rate for 51 pairs of identical twins thus reached 17.7% compared to a concordance rate of zero for the 98 pairs of dizygotic twins.

Case histories available for the nine suicidal pairs indicated the presence of mental illness in several.

A combined follow-up and family study began early in 1974 by Dr. Tsuang and coworkers has resulted in statistics on suicides among 325 patients with manic-depression, 200 schizophrenics, and 160 surgical-patient controls who were admitted to University Hospitals, Iowa City, between 1934 and 1944.

The investigators have now traced all these patients to death or current address, and as of February, 1976, the 352 recorded deaths have included 30 suicides.

Of this total number, 21 were in manic-depressives, eight in schizophrenics, and one in the controls—yielding a rate among the mentally ill approximately five times that seen in the controls.

'Strong Association'

These and other studies have now shown, in Dr. Tsuang's opinion, a "strong association" between suicide and manic-depression, schizophrenia, and alcoholism. He also believes there is "ample evidence" that genetic factors are involved in the transmission of these three conditions, and cited specific findings:

- Manic-depression. Data that he has pooled from seven separate studies of twins indicated a concordance rate of 76% for manic-depression among 156 identical twin pairs but a rate of only 19% among 323 fraternal twin pairs.
- Schizophrenia. Classic studies using the twin method have pointed to a much higher concordance rate for schizophrenia in identical compared to fraternal pairs. In addition, Dr. Tsuang cited a recent investigation, conducted in Denmark by a U.S.-Danish research team, of the incidence of schizophrenia in the biological and adoptive relatives of persons who were adopted soon after birth and who developed schizophrenia.

Among biological relatives of schizophrenic study cases, 8.1% were found to have definite schizophrenia. By comparison, the rate was 2.3% among biological relatives of carefully matched controls. No statistically significant difference was seen between the rates of schizophrenia in the adoptive relatives of the study cases and the controls—1.4% and 3.3% respectively.

- Alcoholism. The same Danish population was used to study drinking problems in 55 men who had been separated early in life from their biological parents, one of whom by study protocol was required to have had a hospital diagnosis of alcoholism.

A total of 18% of these men had themselves been alcoholics at some period in life, compared to only 5% of matched controls without an alcoholic biological parent.

Benzathine Penicillin: Choice Drug for Syphilis

Medical Tribune Report

ATLANTA—Benzathine penicillin G—2.4 million units total by intramuscular injection at a single session—is the drug of choice in the treatment of primary, secondary, or latent syphilis of less than one year's duration, according to the 1976 treatment schedule recommended by the Venereal Disease Control Advisory Committee of HEW's Center for Disease Control here. For patients allergic to penicillin, the committee recommends tetracycline hydrochloride, 500 mg four times a day by mouth for 15 days, or erythromycin, 500 mg four times a day by mouth for 15 days.

For latent syphilis of indeterminate or more than one year's duration, or cardiovascular, late benign, or neurosyphilis, the recommended treatment is benzathine penicillin G, 7.2 million units total by intramuscular injection weekly of 2.4 million units for three successive weeks, or aqueous procaine penicillin G, 9.0 million units total by intramuscular injection of 600,000 units daily for 15 days.

The committee noted that CSF examination is mandatory in patients with suspected symptomatic neurosyphilis.

New ICU Protocol Designed To Avoid 'Quinlan' Dilemmas

Continued from page 1

define "extraordinary life-support measures" as admission to the ICU, blood replacement, parenteral nutrition, vasoactive drug infusions, mechanical ventilation, mechanical cardiac support, cardiopulmonary resuscitation, control of arrhythmias and invasive monitoring. Indeed, the only therapeutic measures allowed are those required for the comfort of the patient.

The new protocol was scrutinized for two years by hospital committees and lawyers. Specifically avoided along the way were vague terms such as "Do not resuscitate," Dr. Loughead said, because this term "can mean anything from withdrawal of all treatment, to total support except if cardiac arrest occurs."

'Total Support' at First

When first admitted to the ICU under the new guidelines, he said, "All patients are assumed to be in the 'Total Support' group until determined otherwise by a complete evaluation. In these patients, everything possible is done to reduce mortality and morbidity."

In the "All But CPR" category fall those patients who "are judged to have irreversible cardiopulmonary failure, or other multiple organ failure, but who still retain normal, or potentially normal, brain function, and who desire, or whose family desires, that efforts be continued."

When the medical consensus is that the case is hopeless, he said, "a firm but sensitive effort is made to educate the patient and the family. When the reality of the prognosis seems to be understood, the patient's status may be changed to the next category."

Meanwhile, he said, every support effort is continued until a cardiac arrest. At that point, "the patient is permitted to die unmolested."

In the third category—"No Extraordinary Measures" are placed patients with minimal brain function and no hope for improvement, such as Karen Quinlan.

"In these cases, extraordinary measures are not initiated, or are discontinued if such discontinuation is not expected to result in immediate demise," Dr. Loughead explained. The decision to place a patient in this group, however, is not solely a medical decision, he stressed. The patient and his family are also involved.

"Patients who have expressed a desire to be spared of sophisticated intensive care because of advanced age, or their own concepts of their disease, may also fall into this group, but are not automatically placed in it. The patient's desire must be evaluated against the medically-defined prognosis. If the patient's concept of his disease is more pessimistic than warranted, re-education and emotional support should be provided."

Further defining who would fit into this category, Dr. Ake Grenvik, another member of the hospital team, said that such patients may be withdrawn from the ICU if they are able to support their own vital functions for a day or two. They have no hope of recovery, he said, and "have lost the reason to be in the intensive care unit. These are patients with severe brain failure, where continued treatment would seem totally meaningless... prolonging death, rather than life."

Nevertheless, relatives of the patient are always involved in a decision to withdraw intensive care. "We approach the relatives when these patients are in coma or don't have a functioning cortex any more, and then if the family agrees with our approach to discontinuing extraordinray measures, we will do this in 100% of cases.

"We do not do it, on the other hand, if there is a disagreement among the closest relatives and the treating physician. It is common for relatives to approach us and ask for discontinuance of treatment, and if we do not agree, we will not go along. So the disagreement, if there is one, can go both ways."

In the case of the last category, "Brain Death," the decision is much easier, both physicians agreed. The so-called Harvard criteria are used here, and if the patient is in that category, all therapy is stopped.

Figures show that of the 577 patients admitted to the ICU in the first nine months since the guidelines were initiated in July of 1975, 482, or 83.5%, fell into the "Total Support" category; 34 patients, or 5.9%, in the "All But CPR" and "No Extraordinary Measures" categories, and 27, or 4.7%, in the "Brain Death" group.

Deaths in the ICU included 39, or 8.1%, in the "Total Support" category; 30, or 88.2%, in the "All But CPR"; 26, or 76.5%, in the "No Extraordinary Measures," and 27, or 100% in the "Brain Death" category.

Some Recover

Most of the patients in the two intermediate classifications died later outside the ICU, Dr. Loughead noted. This included all but one of the "All But CPR." The exception was a young woman with a gunshot wound to the head, with the brain extruding from entrance and exit wounds. "She eventually made a reasonable recovery, although she was left with a severe seizure disorder."

Of the eight patients in the "No Extraordinary Measures" category who left the ICU alive, he continued, "six died in our hospital, one was discharged in a vegetative state to a chronic care institution, and one was eventually discharged home. The latter had a radical laryngectomy, but because the cancer had spread around the carotid artery, it could not be resected completely. He also had severe COPD which led to postoperative acute respiratory failure. It took four weeks to wean him off mechanical ventilation, and another two months before he was discharged home as a respiratory cripple."

The attending physician, the full time ICU team, and other consultants participate in all decisions. The family is also consulted, "but at no time is the family requested to make any decision relating to withdrawal of support."

Medical Tribune

THE GOOD DRUGS DO to better your health

is specially prepared for the waiting rooms of America's physicians to provide patients with accurate information about the medications and regimens their physicians prescribe.

Dr. Louis Lasagna, Professor and chairman, Department of Pharmacology and Toxicology, University of Rochester School of Medicine and Dentistry, is editor of this service.

Each installment features a leading authority on a health problem of concern to the public and to physicians.

Meet Dr. Friedman

Dr. Eli A. Friedman is Professor of Medicine and Chief, Division of Renal Diseases, State University of New York, Downstate Medical Center, Brooklyn, N.Y. He began his specialized work on kidney diseases and kidney failure at the Peter Bent Brigham Hospital in Boston where he was appointed an American Heart Research Fellow in Dr. John P. Merrill's renal training program. Basic kidney transplantation problems were solved during his work under Dr. Merrill.

In 1963 Dr. Friedman was appointed Assistant Professor of Medicine at the Downstate Medical Center. There he initiated on the east coast a new concept in maintenance care for the patient in the terminal stage of kidney failure. As part of this, both long-term hemodialysis and renal transplantation were introduced into Kings County Hospital, which is affiliated with the Downstate Medical Center. Over the years, in collaboration with a vigorous surgical transplant program, the Downstate Kidney Center has received public recognition and federal funding as a prime resource for kidney disease. Its newly designed Chronic Dialysis Unit has proved lifesaving for many.

Dr. Friedman is a Fellow of the American College of Physicians, and former President of the New York Society of Nephrology.

Treatment in kidney failure saves lives

By Dr. Eli A. Friedman

Within the past 15 years we have seen the most dramatic kind of advances in the treatment of kidney diseases, particularly of kidney failure.

Prior to 1960, 100% of patients with uremia died no matter how they were treated—but in 1976, under the best dialysis and transplant programs approximately only 5% will die. We can honestly say that the treatment of the so-called "end-stage renal failure" has undergone a revolution.

A second area of substantial progress has been in the treatment of infections of the kidney, bladder and ureter, which are vulnerable to attacks by bacteria, and are responsive to therapy with antimicrobial agents, especially the newer antibiotics. Thirdly, the management of one of the consequences of kidney disease—namely, high blood pressure—has been eased to the point where even malignant hypertension, once considered a fatal disease, is now manageable and controllable with appropriate medications.

Additionally, in some diseases, the kidneys' involvement in precipitating kidney stone formation or vascular complications is sufficiently understood to be managed medically.

Kidney stone mystery

I do not mean to say that we have conquered all kidney diseases. We still fail to prevent the insidious deterioration of kidney function in certain genetic disorders, like polycystic kidney disease. We remain unable, despite our increased knowledge of how calcium and phosphorus are utilized in the body, to prevent the formation of kidney stones in about two-thirds of known stone-formers. We cannot yet prevent the continuous loss of kidney function in some patients with nephrosclerosis or diabetes mellitus. Nevertheless, the gains that have taken place are far beyond what anyone would have predicted a decade ago.

Unquestionably the most dramatic of our advances in treatment have benefited patients with uremia. The Greek word uremia means urine in the blood, and represents the common, simple explanation of kidney failure. The waste products, which the healthy kidney normally excretes, are retained in the blood, causing illness. Urea is the most obvious of the urine waste substances that accumulate; at least 50 other chemical substances have been identified. Any one of them could conceivably be making the patient sick. Therefore, with all our progress, we must say that we still don't know which chemical substances or combination of "toxins" induce the signs and symptoms of what has been termed the uremic syndrome.

Deficiencies created

We also know that the patient in kidney failure lacks, in the amount present in normal persons, substances that the body needs. For example, some hormone functions of the kidney, such as the secretion of erythropoietin—a hormone that normally acts on the bone marrow to stimulate synthesis of red blood cells—are deficient in uremia. As a result, the patient with kidney failure is anemic.

There are other factors also affecting various body functions. In fact, the complexities of clinical and biochemical aberrations of kidney failure are so numerous that several excellent books have recently been written on the subject. While investigations are continuing, the important thing is that we have already found ways to circumvent otherwise certain death in nearly all patients with kidney failure.

Two startling improvements—one medical and one surgical—are responsible for this great positive change in prognosis. The medical advance was the development in Seattle at the University of Washington by Dr. Belding H. Scribner and associates of a device that permitted repeated access to a patient's blood supply in a newly conceptualized therapy of maintenance hemodialysis. This device, made of plastic, was an external arteriovenous shunt. Attached to the patient's radial artery and vein in the forearm, the shunt allows easy access to the arteries and veins of the patient—and this makes it possible to dialyze or "clean" accumulated wastes from the patient's blood with an artificial kidney two or three times a week on an indefinite basis. Some patients have now utilized this method for 16 years.

Dr. Kolff's kidney machine

The shunt permits the routinized use of the artificial kidney, which had been developed originally by Dr. Willem Kolff in Holland in the 1940s and then perfected by Dr. John Merrill in Boston in the 1950s. The dialysis process repeatedly removes from the blood those waste products of the body that would otherwise prove to be fatally poisonous. The actual technology of dialysis has been substantially improved in the last 20 years. For example, the "hook up" time required for a patient to be connected to an artificial kidney has been reduced to five minutes or less. Disposable tubing makes postdialysis cleanup a ten-minute job.

Evolving simultaneously, the technique of kidney transplantation has proven to be at least an equally great achievement in improving the lot of kidney patients. It had been shown in the early 1900s that a kidney could be transplanted from one animal into another. In 1953, Dr. John Merrill's team at the Peter Bent Brigham Hospital in Boston, demonstrated that, in identical twins, it was possible to overcome the problem of kidney failure in one twin by transplanting a healthy kidney from the other; the transplanted kidney would function promptly and continuously to correct the uremic syndrome.

Further research revealed that kidney transplants need not be limited to identical twins—that other combinations became possible once tissue-matching techniques were worked out and immunosuppression measures clarified. While rejection of the new kidney has not disappeared, excellent ways of dealing with the problem have reduced its importance and made it simply another medical aspect of successful treatment. For example, by the mid-1960s, the development and use of combinations of two immunosuppressive drugs—azathioprine and the corticosteroid, prednisone—made it clear that graft rejection could be greatly retarded. In fact, such rejections could be slowed to the point where large-scale surgical transplant programs for patients with kidney failure became reasonable undertakings. In some centers, 100 or more transplants are performed each year.

How drugs work

Drugs that could suppress the immune response—the body's rejection of anything it considers foreign—play a critical role in kidney transplantation. Initially, when medical scientists first recognized that it was necessary to reduce the effectiveness of the immune system, the drug regimens were poorly understood. Later drugs were developed that made it possible to provide for graduated control of the immune system. Many of these drugs have been used in the chemotherapeutic treatment of cancer. One of the most widely used drugs of this type is cyclophosphamide which will retard skin and kidney graft rejection in animals. Another often prescribed drug is azathioprine, which interferes with rapidly multiplying cells like lymphocytes, the cells most likely to express a rejection response to foreign tissue. A third type of drug employed in suppression of the rejection response is the hormone, prednisone. This drug also reduces the number of lymphocytes throughout the body. Under investigation today is antilymphocyte globulin and antithymocyte globulin, which when developed as a serum in the horse or rabbit, attacks human lymphocytes and destroys their ability to function in an immune rejection response.

These principal drugs are used in various combinations. If a drug has an

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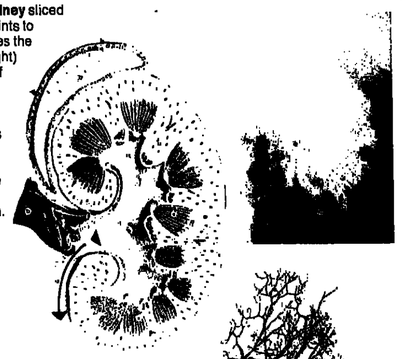

Model shows kidney sliced in half—arrow points to where urine leaves the kidney. X-ray (right) shows network of kidney's arteries after injection of contrasting dye. Specimen shows arterial system. Kidneys filter poisonous waste products from the blood stream.

Why the kidney is absolutely vital

Many people do not understand the absolutely vital role of the kidney, which is second only to the heart in its importance. Its functions are rather startling.

In addition to its vital role in clearing the blood of waste products, the kidney is an endocrine gland, a part of the body's basic defense and growth systems. It secretes some of the major hormones needed by the body, such as erythropoietin, which is required in the bone marrow for making red cells, and several prostaglandins, which were first found in the semen of man and which, among other functions, cause strong contractions of the smooth muscles and certain blood vessel beds.

The kidney also helps to regulate other endocrine glands. For example, about 25% of the insulin daily manufactured by the body is destroyed normally by the kidneys. That is why—strange as it may seem—patients with diabetes who develop kidney failure require less insulin as the kidney failure progresses—the normal kidney wastage of insulin not being present.

In the same way about 25% of the body's normal daily production of glucagon, which is believed to be secreted by the pancreas and to also play an important role in diabetes mellitus, is destroyed by the kidney.

Moreover, the kidney is now recognized as being responsible for manufacturing the active form of vitamin D. In kidney disease, if the patient does not form active vitamin D, a bone problem—which we call "renal rickets," a bending and distortion of the bones—develops. Physicians now know that this isn't due to some poisoning caused by substances being retained in the poorly functioning kidney. It is caused by the failure of the kidney to make this final form of vitamin D. Interestingly, the new synthetic vitamin D substances equivalent to the form finally made by the kidney are being used with increasing success to treat the rickets caused by kidney failure.

For example, we now have available two synthetic vitamin D preparations—and we are able to use them with considerable success in patients with bone disease due to kidney failure.

Blood pressure control

A second major function of the kidney as an endocrine gland is in the regulation of blood pressure. We now understand that the kidney manufactures renin, an enzyme. After being secreted into the blood, renin changes a substance in the blood called angiotensinogen to angiotensin I, which, after conversion in the lung into angiotensin II becomes the most potent substance known for raising blood pressure. Angiotensin also stimulates the secretion of aldosterone by the adrenal gland; aldosterone helps retain

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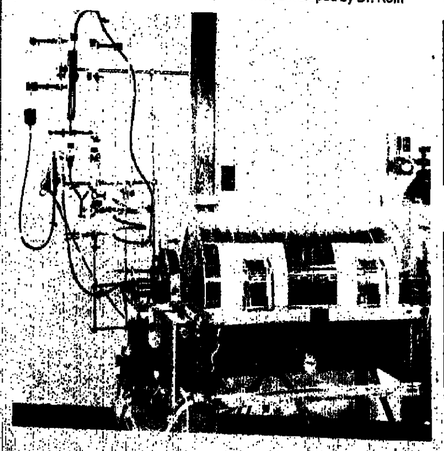
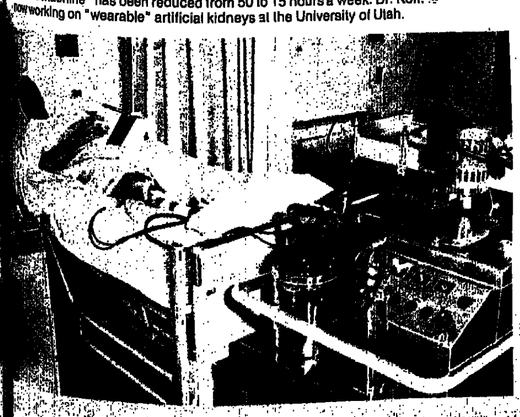
Development of artificial kidney was enormous medical engineering-chemical feat that Dr. Willem J. Kolff began in secret in Nazi-occupied Holland in 1940. Below, a 1947 improvement developed by Dr. Kolff and Dr. John Merrill's team at Peter Bent Brigham Hospital in Boston. In 1950s Dr. Kolff, then at Cleveland Clinic, developed first home dialyzers by adapting Mayteg washer tube (middle). Modern hospital dialyzers (right) are so efficient that time "on the machine" has been reduced from 50 to 15 hours a week. Dr. Kolff is now working on "wearable" artificial kidneys at the University of Utah.





Questions on kidney diseases answered

How many people have kidney failure?
Approximately 50 to 70 persons per million of the United States' general population per year. That's a large number. In Brooklyn and its environs, with four million people, we must cope with about 250 to 280 new patients with kidney failure each year. In addition, people with severe diabetes often develop kidney failure and so do many of those with cancer related to the reproductive and urinary tracts. In most Western societies, it is estimated that as many as 80 per million new patients with kidney failure are produced each year.

Did President Kennedy have kidney disease?
No. He had Addison's disease of the adrenal glands, which sit atop the kidneys. It's believed—for there is pretty good evidence for this—that he was receiving corticosteroid drugs over many years because of the failure of his own adrenal glands to secrete adequate amounts of cortisone.

Do women have more urinary tract infections than men?
Yes. It is estimated that two to four percent of all American women have significant amounts of bacteria in their urinary tracts even though they do not have the usual symptoms of an infection. About five per cent—perhaps as high as ten per cent—of these women will at one time have symptoms of urinary tract infection. But a urinary tract infection does not lead to kidney failure if properly treated.

How do drugs help the patient with a kidney transplant?
Drugs are necessary to prevent rejection of the kidney by the patient's own body. The same body defense mechanism (the immune system) which attacks foreign germs (bacteria, viruses) that cause disease, may attack the kidney which is also foreign to the body. The drugs may thus prevent rejection (attack on the kidney) but they also weaken body defenses against infections and this is a possible hazard.

What happens if a transplant fails?
If a kidney transplant fails (and half of cadaveric kidneys do), a patient can receive a second (or third or fourth) transplant as soon as conditions permit it. In the interval, dialysis treatments are necessary. The annual mortality for transplant recipients is under 10%.

Is a person with a transplant or using a dialyzer able to lead a normal life?
As long as a transplant functions well, the patient will feel and look quite normal. Transplanted patients have babies, water ski, travel everywhere and, indeed, are in a sense "reborn." The stable, well-adjusted transplant recipient is seen in clinic once monthly

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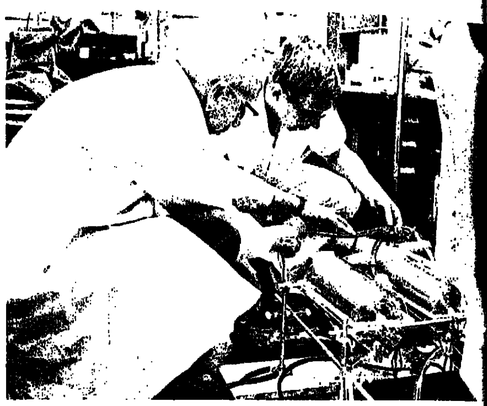
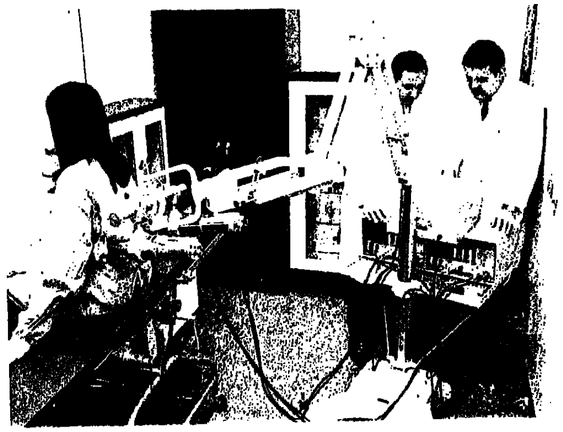
Advances in overcoming kidney diseases

The first physician to connect the kidneys with disease was Sir Richard Bright of London. In 1827 he showed that an abnormal accumulation of fluid within a body cavity or tissues was due to an inflammation of the kidneys. First known as "Bright's disease," it is today called nephritis.

Research proceeded slowly until 1932 when Dr. Harry Goldblatt at Case Western Reserve University School of Medicine in Cleveland showed that clamping the kidney artery of a dog produced high blood pressure. This stimulated research which revealed that kidney disease also plays an important role in diabetes and other disenses.

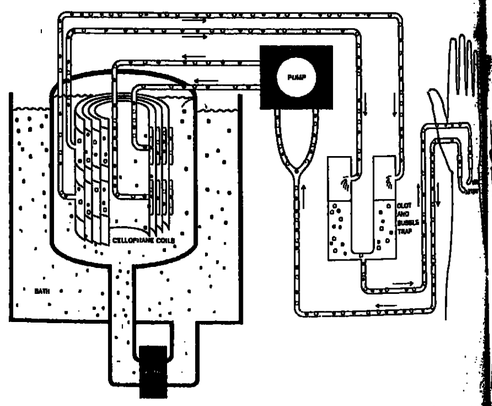
In recent years two lifesaving procedures—kidney transplantation and dialysis—have dramatically altered the once fatal failure of the kidneys.





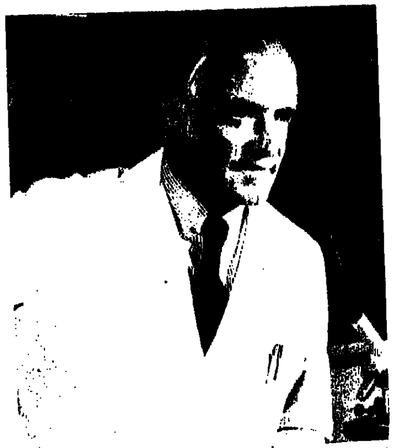
Kidney stones may be revealed by scintillation detector (above). Research at Louisiana State University helped establish that there is a greater incidence of stone formation in many southern and western states, parts of Ohio, Indiana, Illinois and Missouri. Analysis of stones (right) resulted in methods of dissolving some types internally.

Dr. Alexis Carrel (white cap), shown operating at Rockefeller University, pioneered in transplantation, devising techniques still used. In 1902 he transplanted kidney of dog from its abdomen to its neck, connecting kidney artery and veins to appropriate neck blood vessels. It discharged urine through ureter. His methods of connecting blood vessels and nerves won him the Nobel prize in 1912. Working with aviator-engineer Charles A. Lindbergh, he developed a method of preserving donor kidneys until they could be transplanted, and a mechanical heart. He died in 1944 in his native France, accused of being a Nazi collaborator, a charge friends deny.



Artificial kidney pumps blood through the cleansing cellophane coils and chemical baths and back to the body as shown above. The device was first developed by Dr. Willem J. Kolff, the gray-haired physician shown working in the top photo on cellophane coils. Use of the artificial kidney lagged for years because surg... was required to hook up the patient t... the dialyzing machine. Since the n... of blood vessels available was limit... only five to 10 treatments were poss... —sustaining life only for a few week... Then Dr. Belding H. Scribner, of th...

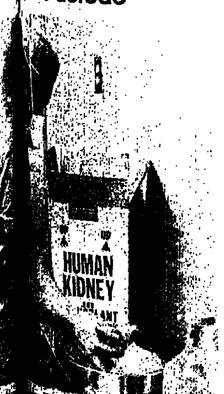
...sity of Washington School of ...cine in Seattle (above), developed ...od of permanently attaching a ...a to the main artery and vein of ...n or leg (top). Later an operation ...vised creating a fistula that elimi... the permanent cannula.



Dr. John P. Merrill (left) led brilliant research at Peter Bent Brigham Hospital in Boston on both dialysis and kidney transplant problems. Tissue matching to prevent rejection of donor kidney emerged as a main transplant concern. Drugs were then developed which reduce rejection reaction to kidneys of nonrelatives.

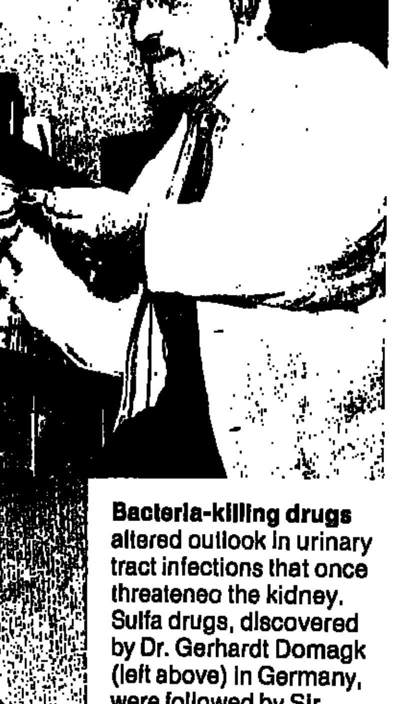
Kidney transplantation, once a dream, has become a lifesaving reality for victims of kidney failure bo... and abroad

First step in transplantation is the matching of tissues (above) of donor and ...ecipient. If they are compatible, next step is removal of donor kidney and ... packing of it in special preservative container. It may then be flown to wherever the pati... is and transplanted. In Europe this is done internationally, with a tissue matching bank...



...Jutland. Newly developed drugs can now largely suppress rejection of the transplanted ...permitting the acceptance of donor kidneys from sources outside of the immediate family.

Controlling urinary tract infections



Bacteria-killing drugs altered outlook in urinary tract infections that once threateneo the kidney. Sulfa drugs, discovered by Dr. Gerhardt Domagk (left above) in Germany, were followed by Sir Alexander Fleming's (left) discovery of penicillin in England and of streptomycin in U.S. by Dr. Selman Waksman.

NEW UNDERSTANDING and the development of new drugs have improved the treatment of urinary tract infections. These infections occur in the largest number in females. It was once feared the bacteria in bladder infections would always ascend to the kidney; modern treatment can usually effectively prevent that.

One of the major advances in our understanding of infections of the urinary tract stems from the work in the late 1950s of Dr. Edward H. Kass, who studied patients at Boston City Hospital. Dr. Kass connected asymptomatic bacteriuria, or more than 100,000 bacteria per milliliter of urine, with the risk of subsequent acute infection of the urinary tract. To grasp what a milliliter is, picture 1000 of them as making up just about a quart of any liquid. He began screening large hospital populations—as well as patients out of hospitals, and special groups of diabetics and nondiabetics, school girls, nuns and other groups—to ascertain how common bacteriuria of this degree was.

Sign of infection

What he found was that schoolgirls, unmarried young women and nuns have bacteriuria in a prevalence of about one to three per cent. He noted that men had a much lower prevalence—a bacteriuria in well under a quarter of one per cent of males. And he was able to show that as women married and had repeated pregnancies, the bacteriuria rate rose continuously to as high as 15% after multiple pregnancies.

Dr. Kass subsequently showed that the detection of bacteriuria in the first trimester of pregnancy, in women who have at that time no symptoms of a urinary tract infection, presages the development of symptomatic urinary infection in a significant number of these women at the time of delivery. If, on the discovery of the presence of bacteriuria, pregnant women were treated with a sulfa drug, it was possible to prevent the conversion to clinical urinary tract infection at delivery.

Perhaps even more important in some respects was Dr. Kass's demonstration of an association of premature births with the presence of bacteriuria. Since then, in large population studies in Jamaica in the West Indies and in the United States itself, the persistence of bacteriuria of 100,000 organisms per milliliter has also been associated with higher blood pressure than in patients who do not have such a bacteriuria.

Today most patients first come into contact with the concept of bacteriuria during a pregnancy screening urine culture or some other form of routine health check. When the doctor discovers bacteriuria, his course is to try to prevent the development of a clinical urinary tract infection. In earlier years the asymptomatic patient was not treated until the advent of a full-blown urinary tract infection.

A wide range of drugs is available to combat urinary tract infections. The sulfanilamide drugs were discovered in the 1930s by Dr. Gerhard Domagk in Germany, who won a Nobel prize for his work. Before World War II these drugs were introduced in this country by Dr. Perrin Long, Johns Hopkins School of Medicine, who was later Chairman, Department of Medicine, Downstate Medical Center.

After World War II, penicillin, the discovery of Dr. Alexander Fleming in England, became available for prescription. Then in the late 1940s, streptomycin was found and, by the early 1950s, we had the tetracycline drugs.

Control of infection

Today, although there are many drugs for the treatment of acute urinary tract infections, the sulfa drugs remain among the major standbys. In most cases—about 97% of the uncomplicated cases of urinary tract infection—the infection will respond to either the sulfa drugs or a derivative of penicillin called ampicillin.

Because we have several good drugs available, a ten-day to two-week course of therapy can control most of the previously distressing and sometimes debilitating infections in young women—even for the fourth or fifth infection in a schoolgirl. Today it is relatively rare for such an infection to become chronic. If it does, it may require six months or even a year of antimicrobial therapy.

One thing we do not see very often today is tuberculosis of the kidney, once a serious cause of kidney failure, which has been brought under control with modern antituberculous drugs.

Although about 90% of all urinary tract infections occur in women, about 60% of all renal failure occurs in men—who seldom have urinary tract infections. This is an important statistical finding because it indicates that urinary tract infection is not the principal cause of kidney failure. No woman should feel that a urinary tract infection will automatically lead to kidney failure. With proper treatment her urinary tract infection will in nearly all instances disappear in a few weeks.

What your doctor can do

IN CONSIDERING the possibility of kidney infection, the physician must first make a diagnosis and then follow up with the appropriate antimicrobial drug treatment. Today we have excellent means of carrying out both these functions.

When the problem appears to be kidney failure, the physician's job is more complicated and prolonged. The first thing that the doctor can do is to try—in collaboration with a kidney specialist (nephrologist)—to define exactly what the kidney problem is. If there is unexplained proteinuria—an excessive amount of protein elements in the urine—a kidney biopsy may be required and then analyzed so that it can be determined whether it is treatable.

Secondly, your physician may want to make an inventory of the ability of your kidneys to clear waste substances. There are many techniques for doing this. One of the most widely used is called the endogenous creatinine clearance test, which involves collection of the urinary output for a timed period—usually 24 hours—but it may be as short as six hours. It also requires a blood test. With it your physician can estimate the rate at which the kidney disposes of waste. This helps to determine what course needs to be followed.

Search for damage

Thirdly, your physician's examination will reveal whether there has already been any other adverse effect from kidney damage and the extent of it. For example, he will check to determine whether there is any bone disease such as hyperparathyroidism, or impairment of nerve function, which has developed as a complication of kidney failure.

Lastly, if it appears that kidney failure has developed, your physician can help, working with a medical kidney specialist or a transplantation surgeon, in making sure that a "life plan" that is suitable to your problems and circumstances is worked out. There are many things in a transplant program which your physician may assess. If your brother or sister wishes to donate a kidney, then he or she needs to be evaluated. This means that everything from blood type to tissue type as well as the possible presence of diabetes or other disease must be checked out so that if a transplant is needed, it can be done with a minimum of stress and tumult.

The physician also can greatly help in answering the questions of the patient and his family regarding dialysis and transplantation. These are procedures that millions of people are becoming aware of in many different ways. Today millions of people have actually seen a successful kidney transplant performed on television. They have seen similar programs on dialysis. But while these educational programs provide a great deal of general information, they cannot give the person with kidney disease the specific personalized information that he needs in terms of his own kidney problems. For that sensitive briefing everyone should turn to his family doctor.

Dr. Eli A. Friedman checks the dialysis equipment of patient.

Dialysis and transplantation work together. Virgil Mayes, shown measuring dialysis ... at University of Southern California Medical Center, later underwent successful transplantation. If that failed, he could return to dialysis or get another transplant.

What you can do to help yourself

THE MOST IMPORTANT THING you can do if you suspect you have some kind of kidney or urinary tract problem is to go to your physician for an examination and evaluation of your difficulties. One of the things you must be clear about is that urinary tract infection does not lead necessarily to kidney failure, the symptoms of which are often quite different from those of urinary tract infection.

Important symptoms

To discuss these two different problems separately, let's begin with the urinary tract infection. In the adult with a urinary tract infection, the patient usually notices a need to void frequently and with some degree of urgency. You may develop a pain in the side below the ribs or in the lower central back. You also may notice pus, mucus or blood in the urine and that you have a fever—as high as 104°F. When such symptoms are called to your physician's attention, he can make a proper diagnosis from a urinalysis and urine culture and prescribe an appropriate antibacterial medication, to check the infection.

It is important, then, to follow the medication schedule prescribed by your physician, which is based on delivering a bacterial killing dose of drug throughout the day into the kidney and bladder. Usually your physician will tell you to drink extra amounts of fluids consisting of water and fruit juices, as much as two quarts daily. With such treatment the infection will be cleared up quickly, symptoms being relieved by the third day and bacteria disappearing from the urine in 10 days.

Infection in child

A urinary infection in a child is harder to recognize because the child is unable to say what is wrong. But if the child complains of voiding pain, abdominal discomfort or develops an unexplained fever, these signs may be clues to a urinary tract infection and the physician should be informed.

To turn to the problem of renal failure attributable to urinary infection: for many years there has been a debate over the idea that repeated acute or sustained chronic urinary tract infections will ultimately induce irroversible damage to the kidneys. However, this belief has not been substantiated and some clinical experience suggests that the outlook may be less grim. A woman with acute urinary tract infections is not likely to develop any loss of kidney function or kidney failure if her infection is properly treated. In fact, a clear link between urinary tract infection and kidney failure is not easily made.

Moreover, there are warning signals of kidney disease. You should see your physician if you notice blood in your urine. You may also notice an unexplained urgency in the need to urinate or increased frequency, sometimes at night (or unexpected and continued bedwetting in a child). You may also feel irritable and unable to find a comfortable position in sitting because your back hurts.

All these may be clues to kidney disease or to diabetes mellitus. Therefore you can help yourself by calling to your physician's attention any change in habits of urination, frequency, pain, or blood in the urine. He may want to test you for diabetes. But these signs and symptoms of kidney disease are not necessarily indications of kidney failure, which is relatively rare.

The development of kidney failure may be insidious—perhaps starting with edema—a swelling of the feet and ankles. You may notice an intolerance to cold. You may feel exhausted. You may feel nauseated and not be able to sleep well at night—and then feel drowsy all day. You may also develop some discoloration of the skin—an orangish yellow color to the skin. You may also notice some twitching and jumping of your legs and arms.

All of these are signs of kidney failure—but you need not be frightened to the point of panic. Today kidney failure is treatable, often reversible, and for most other patients manageable to the point of satisfactory rehabilitation.

But you do need to see your physician and follow his instructions. The critical step in diagnosis and treatment is your recognizing that something is wrong and seeking expert attention.

Helping in adjustment

The news that you have "end stage" kidney (renal) failure can be shocking and depressing, even though you may have been aware for years that your kidneys were steadily losing their ability to function. It is hard to shake the feeling that you felt it would never get so bad as to threaten your life. But when that is clear, you are faced with the problem of adjusting to what will be a complex treatment plan.

Such an adjustment is difficult emotionally. But you will have working with you specialists in kidney problems: surgeons, urologists, nurses, nutritionists and social workers. They will collaborate in devising a life plan that is tailored to your specific needs, helping you meet the physical and emotional problems of transplantation or dialysis. You will play an active role in managing your own care—and have the prospects of being able to live and enjoy your work and family life.

What you can do to help yourself is to ask questions. The more you know about all aspects of your treatment, the better will you be able to create a satisfying life for yourself.

Two most famous victims of kidney failure: Jean Harlow and Howard Hughes

There were no artificial kidneys or kidney transplants when Jean Harlow, who starred in Howard Hughes' movie, *Hell's Angels*, died of kidney failure in the late 1930s. But they were available when Hughes, who had become a mysterious recluse, fearful of doctors and medicine, died in 1976 of the same thing. Although Hughes gave millions for medical research, he died as a result of his pathological fear, refusing medical attention. Ironically, by that time, artificial kidneys had become available to anyone at Government expense.

Treatment in kidney failure saves lives

Continued from page 19

application in cancer chemotherapy, it has probably also been tried to prevent kidney transplant rejection.

The impact of these developments has not been limited to kidney disease. What has been learned in kidney transplantation has contributed to efforts to transplant other organs. Because it is a paired organ and a person can live well with only one kidney, kidney transplantation offered a means of developing modern organ transplantation.

One aspect of kidney transplantation that may be underappreciated is how the medical and surgical new developments are applied together. For example, should there be a period of rejection of the new kidney, the patient doesn't die suddenly as he would if the heart were being rejected and stopped beating. Instead, knowing that rejection is a reversible phenomenon that can be treated by drugs, dialysis is begun to support the kidney transplant patient during this period of rejection. Thus dialysis and kidney transplantation can frequently be combined.

Why the kidney is vital

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sodium in the body when it is needed.

The kidney is the principal regulator of the body's salt and water—as anyone knows who drinks a few beers on a Saturday night; within a few hours the extra fluid passes through the kidneys into the bladder and out. If the kidney is not functioning properly—and you drink the same three beers—the excessive fluid accumulates in the body. If you were to keep on drinking and the kidney did not function, you would go into what appears to be heart failure—except it is not heart failure because of anything wrong with the heart. The trouble lies in the inability of the kidney to excrete this extra fluid—causing the overloaded heart pump to fail.

We know that one of the principal nitrogen waste products in urine is urea. The stool contains only small amounts of nitrogen waste—let's say only a gram a day, whereas the urine may contain as much as 50 grams. (There are a little less than 30 grams in an ounce). This provides a clue to what may happen in kidney disease. In kidney failure, one of the easiest and first things to be checked is how much nitrogen waste, urea, has accumulated.

Still another important role of the kidney is in regulating the body's acid base balance. Together with the lungs, the kidney regulates the body's balance between alkalinity and acidity. In kidney disease, acidosis usually develops for two reasons. One is that the kidney normally secretes acid. In kidney failure this ability is impaired. Second, some of the waste products of the chemical conversion of protein substances—the sulfates and phosphates which are normally excreted—are retained, causing an acidosis.

Questions on kidney diseases answered

Continued from page 19

or less. No "solution" for renal failure provides a result as good, or a patient as healthy, as a well-functioning kidney transplant. Well-dialyzed patients similarly are able to work, study and care for their families.

Can dialysis be done at home?

Many patients, if they wish to, can learn to perform their dialysis at home. Others will prefer treatment at an outpatient facility. The freedom and self-control of home dialysis facilitates emotional tolerance and full rehabilitation.

How often is dialysis needed?

Usually two or three weekly treatments, four to six hours each, are sufficient to sustain a relatively good condition.

Aren't people afraid of being hooked up to a machine and dependent on it?

Adjustment to maintenance hemodialysis can be difficult emotionally. The thought of dependence on a machine week in and week out can obviously be depressing. Many times, the dialysis patient doesn't feel "quite well" and lacks spark and drive. Overall, however, the treatment regimen is quite bearable—many patients are now in their fifth to tenth years. Such patients can function as professionals, housewives, and students and live personally fulfilling lives.

Dialysis patients may have their names placed on a transplant waiting list. The annual survival of uncomplicated (no systemic disease) patients on dialysis is about 95%.

How long can someone live with dialysis treatments?

No one knows. Patients who started on dialysis fifteen years ago, when the treatment first became available, are still living and well. It's interesting also to note that those patients originally needed to spend as many as fifty hours a week on dialysis. In less than ten years we are now down to fifteen hours a week, on the average. Dialysis is getting faster, better, and safer as we learn more about it.

Does the Government pay for dialysis, if necessary?

On July 1, 1973, almost all kidney patients in this country became eligible for U.S. Government Medicare coverage. Age and income are not determining factors. Anyone who has worked under Social Security long enough to be insured has coverage, which begins after the patient has been on dialysis for three months. There is no waiting period for a transplanted patient. Approximately 80% of all reasonable costs will be paid by the Federal government. Other types of complementary insurance will usually pick up the 20% balance. The patient on Medicaid need not worry, for the 20% is fully covered. Costs for treatments and medical care have ceased to be a practical problem for nearly all patients.

While his mother's dialysis clears her blood, her son adjusts tubing. Kidney centers, such as that at Downstate Medical Center, Brooklyn, train family in home dialysis.

What the family can do to help you

There are few diseases in which the help of the family is more critical to the patient than in kidney failure. That is why, if you should develop kidney failure, your family will be called upon for help in planning and devising the most individualized way for you to overcome the failure of your kidneys.

Initially, the family can greatly help the person with kidney failure deal with the shock—often bewildering and depressing—of realizing that he or she has lost a long battle with dwindling kidney function and now must turn to either transplantation or continuing dialysis to survive. In such a situation the family can, with the help of skilled counselors at the kidney disease centers throughout the country, help the patient deal with this emotional shock—and learn what is involved and what is the best long-term plan.

Possibilities available

The family, too, has to face the problem, and by doing so calmly, by participating constructively in the planning of each step, can greatly relieve the patient's anxiety about his or her future—and theirs.

One of the first possibilities that comes to mind is the transplantation of a kidney from some member of the family—parent, brother, sister or child. Often someone in the family immediately wants to rush in as a "donor." However, the problem is more complex than that. Just as blood must be matched for type in a blood transfusion, there must be a matching of tissue. There must also be an examination of the health of the donor—and consideration of how well the donor can manage with only one kidney. Certain conditions, like diabetes or high blood pressure, would make it seem too risky for some people to donate a kidney.

Fortunately, there are other donor possibilities. One of them is that a cadaver kidney may be utilized. At present relatively few patients who desire a cadaveric kidney get one, because of the small number of kidneys being donated. Attempts are being made to increase the number of people who donate their kidneys after death for this purpose. The lack of donated kidneys limits long-term planning to one of two situations: either a transplant from a living donor whose tissue appropriately matches the patient's, or maintenance of the patient on hemodialysis—a process whereby a dialysis machine carries out the cleansing of the blood that the kidneys ordinarily do.

Family plays big part

In both of these processes the family is very much involved.

In transplantation of a kidney the outcome depends mainly upon the patient's condition and that of the source of the kidney. In the best circumstances, in which the kidney failure patient has no systemic disease affecting other organs, and receives a perfectly matched kidney from a healthy brother or sister, the chances are close to 100% that that kidney will be functioning well three to five years later. However, it is more common to receive a "compatible"—not perfectly matched—kidney from a parent, child, brother or sister and one can count on about an 80% chance that it will be working well two years later. Medical records also show that if a cadaveric kidney is transplanted, the kidney will have been rejected by the body by the end of two years in about 50% of the cases. What can then be done is to transplant another cadaveric kidney—even a third or fourth or fifth time. In between transplants, dialysis is required.

It is because all this is a long and complex problem that the understanding, knowledge and support of the family is very important. For example, the big hazard for the kidney transplant patient is infection, because the drugs which keep the body from rejecting the kidney also reduce the body's defenses against infection. Thus the family can play an important role in reducing the risk of infection at home.

As long as the transplanted kidney functions well, the patient will feel and look normal. People with transplanted kidneys can have babies, swim, water ski, drive, travel and work. Once a month, the well-adjusted transplant patient comes to the kidney clinic for a checkup. No "solution" for kidney failure works as well as a good kidney transplant—and family cooperation helps achieve a healthy adjustment.

However, transplantation is not the treatment modality selected by everyone. Many patients, after working out the situation with their family, their doctors, and staff of the kidney center, elect to rely on an artificial kidney machine for maintenance hemodialysis. There are today dialysis machines which greatly simplify this method of extracting wastes from the blood. For example, the dialysis machine may be kept at home. This permits scheduling treatments to suit the individual rather than a center's needs.

The patient usually requires two or three treatments a week, each of which lasts four to six hours. Often family members can greatly help make this tolerable. Well-adjusted home dialysis patients continue functioning as teachers, lawyers, salesmen, mechanics, physicians and in most occupations.

However, sometimes patients become depressed by being dependent on a "machine." The idea of needing to rely on it for years is not an easy one to adjust to. In addition, the dialysis patient often doesn't feel "quite well" and may periodically lack drive, and this, too, worries him. It's important for family members to help the patient cope with his "down" feelings.

24,000 use dialysis

When faced as a family problem, maintenance hemodialysis can be incorporated into a routine that will permit a satisfactory "coming to terms" with the illness. For the 24,000 Americans "on dialysis" today, efforts to improve the quality of life are continuously making a good therapy better. Dialysis patients who have no living donor may have their names placed on a waiting list for a kidney transplant.

Some patients who started on dialysis 16 years ago are alive and well. In recent years the dialysis machines have become more efficient—so that the time on the machine is down from 50 hours a week to about 15.

Obviously the physicians, kidney specialists, nurses, social workers and others can manage the medical aspects and the Government pays for most of dialysis costs. But it is usually only the family that can make it all worthwhile.

Training makes family members expert in management of home dialysis.

Brain Surgery May Relieve Seizures in Intractable Epilepsy

Medical Tribune World Service

TORONTO—Partial or complete forebrain commissurotomy in 10 epileptics intractable to medical management has greatly improved seizure control in seven, one of whom now has "no further abnormal electrical activity," Dr. Alexander Reeves reported here.

Four patients had "excellent results," three having no seizures on follow-up of up to four years. The fourth had seizures three months after surgery due to a concussion, but none later, Dr. Reeves told the American Academy of Neurology.

Of three patients with "significantly improved" control, two have experienced decreased frequency of seizures, and the third, who had generalized tonic-clonic seizures at least once a week, now has them modified to complex partial seizures, said Dr. Reeves, who is chairman of the section of neurology at Dartmouth-Hitchcock Medical Center in Hanover, N.H.

As a result, the neurosurgeon expressed "guarded optimism that forebrain commissurotomy may be a useful therapy" for intractable epilepsy.

All patients "had been incapacitated for at least four years despite closely supervised medical therapy and none were considered candidates for standard neurosurgical procedures," he said. All had EEG or other evidence of a lateralized disorder.

"Three patients had complete forebrain commissurotomy (division of the entire corpus callosum, the hippocampal commissure, the anterior commissure and one fornix); five patients had frontal commissurotomy (division of the anterior two-thirds of the corpus callosum, the anterior commissure, and one fornix); and two patients had complete division of the corpus callosum and hippocampal commissure."

All but one patient have remained on anticonvulsants though frequently at lower dosages. The one on no medication is also seizure-free four years after complete forebrain commissurotomy, Dr. Reeves noted. Preoperatively, this patient had right cerebral hemiatrophy and suffered 20 or more complex partial or generalized tonic-clonic seizures a day.

Two of the three failures in the series continue to have as many or more seizures following surgery, he also reported. The third failure, who underwent frontal commissurotomy, died 12 days later. Autopsy revealed "focal frontal cortical vein thrombosis with cerebral infarction," Dr. Reeves said.

Award Winner

Medical Tribune Report

HOUSTON, TEX.—Dr. Howard E. Skipper, President of the Southern Research Institute, Birmingham, Ala., received the 25th annual Ernst W. Bertner Award "for distinguished contributions to cancer research." The award is presented annually by the University of Texas M.D. Anderson Hospital and Tumor Institute here.

INTERNATIONAL REPORT

from Germany *from the Editors of Medical Tribune Germany, Wiesbaden*

New Test Facilitates Study of Acute Intermittent Porphyria

Medical Tribune World Service

ERLANGEN, GERMANY—At a meeting of the Medical Association here, Dr. K. F. Druschky of the Clinic for Nervous Diseases here stated that many drugs currently in use may trigger the onset of acute intermittent porphyria (AIP), so that a quite simple method of determining the activity of an enzyme for identification also of latent AIP patients represents an advance for patients concerned. Current estimates show that at least 1000 patients in Germany suffer from known AIP. About 50% of their approximately 25,000 relatives may be carriers of AIP gene, since this is a hereditary autosomal dominant disease. It has not yet been possible to devise a specific therapy for this disease, and every acute seizure consequently represents a serious threat to life.

Data on 42 AIP patients yielded reduced uroporphyrinogen-I synthetase (Uro-I-S) activities between 0.32 and 0.63 IU. Only 15% of a control group of 207 healthy subjects fell below the 0.65 IU limiting value; above that there were no porphyrin metabolism disorders. There was a significantly higher proportion (40% of the test data values) in the pathological area in 172 relatives of IAP patients, where those subjects presented neither clinical symptoms nor increased excretion of porphobilinogen and δ-aminolevulinic acid, thus eluding the conventional methods of detection as carriers of the gene.

As the patient's life is endangered with every seizure, medical requirements for prevention demand examination of the porphyritic's family in every case. The patient himself should be provided with an identity card stating

Continued on page 32

Miniaturized ECG Recorder Developed in Switzerland

This Swiss-manufactured "Minigraph," weighs under 800 g, is battery powered. All standard limbleads can be recorded. Chart is readily replaced.

from France *from the Editors of Tribune Medicale, Paris*

Modern Diuretics Useful in Congestive Heart Failure Therapy

Medical Tribune World Service

RABAT, MOROCCO—At a symposium on modern diuretic therapy in hypertension here, Professor Jean Di Matteo, a cardiologists of the Hôpital Necker, pointed out that the third generation of diuretics has revolutionized the treatment of congestive heart failure. Coming after acetazolamide, the thiazides and the anti-aldosterones have permitted the reassurance of hypertensive patients of prolonged survival in appreciable comfort. However, no diuretic is perfect and combinations of different kinds are generally more active and better tolerated than any one agent. Renal insufficiency, organic or functional, modifies diuretic action and necessitates a precise adaptation of the treatment to each patient, regular tests and supervision.

In obvious congestive heart failure, according to Professor Di Matteo, diuretic treatment must be used in conjunction with the traditional prescriptions: rest, a salt-free diet, digitalization. A diuretic should be prescribed with care: it must be effective without being excessive, complications arising most often from an overdose.

If moderate congestive heart failure is not accompanied by a renal crisis, most investigators agree on the advisability of a thiazide of average diuretic activity, Professor Di Matteo said. However, potent diuretics, such as furosemide and ethacrynic acid, which readily induce an extra-cellular dehydration, can be used, at the outset of treatment, in extensive congestive heart failure.

Hypokalemia, which may be induced by diuretics, can be prevented by systematic administration of potassium chloride per os. Yet the logical thing would be to combine the thiazides with diuretics that spare potassium. These diuretics counterbalance the potassium depletion brought on by the thiazides and are anti-aldosterones. Regardless of the posology and the diuretic prescribed, it should be administered in the morning so as to avoid nocturnal polyuria.

The thiazides are only slightly effective in the case of a renal insufficiency, even if the diuresis is maintained. Diuretics that spare potassium are contraindicated in principle, lest the already

Continued on page 32

from Britain *from the Editors of Medical News-Tribune, London*

Vaccine Rapidly Controls Pseudomonas Infection in Burns

Medical Tribune World Service

BIRMINGHAM, ENGLAND—A vaccine that is effective within 24 hours against *Pseudomonas* infection in severe burn cases, is now ready for a large scale clinical trial, reports Dr. J. P. Bull, MRC Industrial Injuries and Burns Unit, Birmingham Accident Hospital.

It has been developed over the past two years at the unit by R. J. Jones, Ph.D., and E. A. Rowe, Ph.D., and will be produced commercially by Burroughs Wellcome.

Dr. Bull said: "In our experiments with animals, burns that in themselves carry negligible mortality but when infected with *Pseuromonas aeruginosa* have a mortality of up to 80 per cent, are cured by the vaccine.

"We have tried out the vaccine on ourselves, following the changes in the various antibody responses and red and white blood cell responses. In a project

Continued on page 32

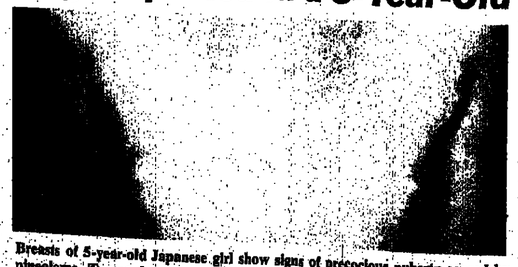
from Japan *from the Editors of Medical Tribune Japan, Tokyo*

Precocious Puberty Reported in a 5-Year-Old Girl

Medical Tribune World Service

TOKYO—A rare case of precocious puberty due to pinealoma in a young girl was described by Dr. Nagao Kubo, of the Neurosurgical Center, Tokyo Women's Medical College, here at the ninth annual meeting of neurosurgeons to discuss special problems in that field in Japan.

A five-year-old girl had an onset of generalized spasm in December, 1974, reported Dr. Kubo. Subsequently, she occasionally complained of a headache in the region involving the left occiput and medium vertex. On July 28, 1975, she complained of a sustained intensive headache with three episodes of vomiting. Her headache failed to respond to prescribed analgesic on July 31, and the subsequent EEG proved positive. The symptom persisted after an antispasmodic therapy.



Breasts of 5-year-old Japanese girl show signs of precocious puberty caused by pinealoma. Tumor, later removed, also caused spasms, headache and vomiting.

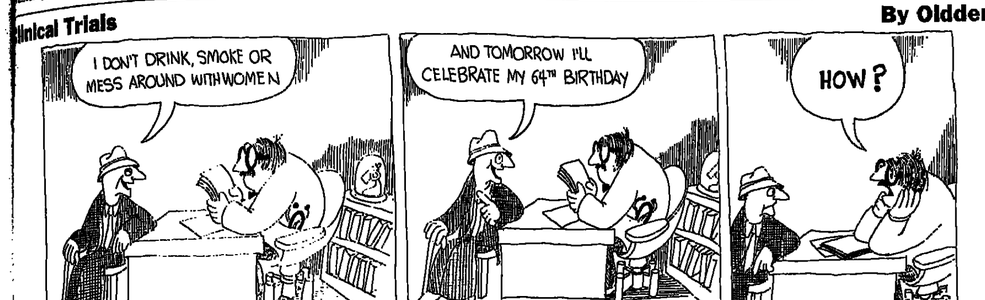
On Aug. 5, the patient was admitted to the pediatric clinic of the college hospital. Because of the presence of congested papilla, she was referred to the neurosurgical clinic of the center.

Findings after admission included clear neurological consciousness, slight lethargy, and marked bilateral papillary congestions. An induration re-

Continued on page 32

Clinical Trials

By Oldden



89% Complete Remissions Achieved in Cancer of the Testes by Chemotherapy

Continued from page 1

plete remission, thus bringing the complete remission rate to 89% (25 of 28).

The chemotherapeutic regime, which Dr. Einhorn described as "rugged," began with five daily 15-minute IV infusions of cisdiammine dichloro-platinum (cis-platinum), every three weeks for three courses, with vinblastine on the first and second days of each course. On days two, nine, and 16 of each platinum course, bleomycin was also given, and continued weekly for a total of 12 weeks. Dr. Einhorn also gave BCG immunotherapy to patients who achieved complete remission.

Maintenance therapy consists of monthly vinblastine and BCG.

During the 12 weeks of intensive chemotherapy, the patients experienced serious side effects, but careful monitoring and supportive care kept the effects manageable. "Especially in patients who had been treated with radiotherapy, anemia and leukopenia were problems, and all patients experienced a severe drop in their white blood count during the second week of chemotherapy," Dr. Einhorn said. "Where infection occurred, we gave broad-spectrum antibiotics."

Other side effects included nausea and vomiting, weight loss, and loss of hair, all of which were limited to the first 12 weeks of therapy. "Three patients developed kidney problems, a result of the platinum therapy, but we were able to correct the trouble and resume chemotherapy. No patient shows any residual nephrotoxicity," said Dr. Einhorn.

"Today, 12 of the 16 complete remissions in the study group, and all seven of the additional complete remissions remain alive and disease-free from six plus to 18 plus months with a median survival of nine plus months," Dr. Einhorn concluded.

TV Series Promotes Health Knowledge

In "Breathing Made Hard" (top), Mario Machado, the host of television's *Medix* series, undergoes respiratory test to demonstrate that nonsmokers are less susceptible to respiratory disorders than smokers. Above, Mr. Machado demonstrates new apparatus in "Biofeedback: Waves of the Future," a *Medix* segment that shows how biofeedback therapy is used in migraine, epilepsy, insomnia, back pain, and paralysis. The Emmy Award winning series on medicine and health, returning to its second year of national broadcasts, will also investigate weight loss, sex, child abuse, and poisoning.

Disulfiram Is Not 'A Deadly Poison,' Says Expert on Alcoholism Therapy

Medical Tribune Report

MIAMI—It is time to bury the myth that disulfiram is "a deadly poison," Dr. Ruth Fox asserted here, noting that many alcoholics are afraid to take the drug and many doctors still refuse to use it.

"It is not a dangerous drug when used properly," the New York psychiatrist told the American Psychiatric Association, warning, however, that disulfiram "should be prescribed only by a doctor who should give careful and minute instruction about its use with a detailed description of the reaction that would occur if the patient did drink either knowingly or inadvertently."

Disulfiram works by enzyme interference, preventing normal digestion of alcohol so that there is a build-up of acetaldehyde, Dr. Fox stated.

She noted that the dose has now been reduced all over the world to 500 mg daily for five days, then 250 mg daily thereafter. A University of South Carolina team concurred that "much of the fore of the disulfiram effect comes from the time when [a higher] dose was utilized."

In their recent study of the effects of the drug on behavior, for example, Dr. Martin H. Keeler, Dr. William C. Miller and Dean G. Kilpatrik, Ph.D., of the university, concluded that disulfiram, administered in doses of 250 mg per day for one week, did not precipitate depression in a group of subjects selected on the basis of absence or depression. The reason for the study was the fact that disulfiram inhibits dopamine beta hydroxylase as well as aldehyde dehydrogenase. Decreased availability of norepinephrine at synaptic clefts as a result of the hydroxylase inhibition has been thought responsible for depression.

Dr. Fox, who has treated 4,000-5,000 alcoholics since the early 1930's, attested to the "great value" of disulfiram and to its "absolute safety" if it is carefully monitored in the first few weeks or months of therapy and if the patient is cooperative. Emphasizing that patients should be warned about certain foods and drugs that contain alcohol, she offered the following guidelines:

- Crepe suzettes or "fruit swimming around in brandy" should not be eaten. However, foods cooked with alcohol are safe if the alcohol has been volatilized by the heat.
- French salad dressing containing wine vinegar can be used sparingly.
- Shaving lotion and underarm applications can be used safely but guardedly. Alcohol rubs should not be used.
- It is safe to take one teaspoon of cough syrup every four hours providing it does not contain more than 10% alcohol.
- Engineers should not go near large open vats of alcohol and painters should be sure a room is well ventilated if they are shellacking a floor.

Dr. Fox stated that in her opinion disulfiram does not work simply because it engenders fear of drinking but "because it also cuts down the overwhelming conflict an alcoholic goes through when he is trying to control his alcohol intake. If he were not on disulfiram, he might have to say 'no' to the impulse to drink several hundred times a day when in the throes of a drinking period. When he is on disulfiram, however, there is no such conflict for he knows he cannot drink for at least five to seven days after his last pill without becoming ill."

Laser Therapy Swiftly Controls GI Tract Bleeding

Continued from page 1

included gastric and duodenal ulcers hemangiomas, angiodysplasia of the large bowel and GI carcinomas.

The findings were detailed by teams at Beth-Israel Hospital, New York, the University of Southern California, Los Angeles, and the University of Erlangen-Nuremberg, West Germany.

Dr. Albert M. Waitman, who led the Beth-Israel group that pioneered in some of the basic technical and animal endoscopic laser studies, noted that refractory lesions hitherto out of reach to non-surgical procedures have now become accessible to the laser beam.

In the Beth-Israel procedure, which is basically that employed by all of the groups, a 2.5 watt water-cooled argon laser is coupled to a standard endoscopy unit. The laser's fiber bundle is sufficiently flexible so that it doesn't impair the normal positioning of the endoscope, the investigator said.

"In treatment, the tip of the scope is manipulated until the bleeding site is seen," Dr. Waitman reported. "The guiding beam is then aimed and the laser force discharged. The tip of the fiber is held 2 cm from the surface of the lesion, and a spot size of 5 mm is slowly moved across the bleeding defect until all bleeding has ceased. The procedure requires three to six minutes, depending on the size of the defect and the amount of bleeding."

Dr. Waitman observed that tissue damage produced by the laser beam is "remarkably limited to superficial layers of the gastric wall and does not interfere with the reparative process."

A major advantage of the procedure, he added, is that "One can decide to do laser photocoagulation at any time during endoscopy, once the bleeding site has been identified." He said that the Beth Israel group plans to add a jet of CO_2 gas to the procedure, in order to blow blood out of the base of a crater formed by a bleeding lesion. This step will make it possible to coagulate the base of the lesion more readily.

The Beth Israel group's initial clinical series included four patients whose bleeding lesions were due to hereditary telangiectasia, uremic gastritis, chronic gastric ulcer and carcinoma of the stomach, respectively. The patients have been treated a total of 13 times to coagulate 35 to 40 bleeding sites or to control rebleeding.

Dr. Waitman stressed that the procedure has been attempted only in patients in whom surgery has failed or is no longer possible. His findings were detailed in a lecture, an exhibit, and an interview. Coauthors were Drs. Ian Spira, C. P. Chryssanthou and Richard Stenger.

In the German study, reported by Dr. Peter Fruhmorgen, endoscopic laser coagulation was "successfully employed" in 10 patients with hemangiomas, angiodysplasias of the large bowel, bleeding incomplete gastric erosions, a hemorrhaging gastric ulcer, and a bleeding duodenal ulcer. The procedure was ineffective, however, in stemming a massive arterial hemorrhage from an inoperable gastric carcinoma.

Dr. Fruhmorgen said that, on the basis of these trials, the group is now employing endoscopic laser therapy "routinely."

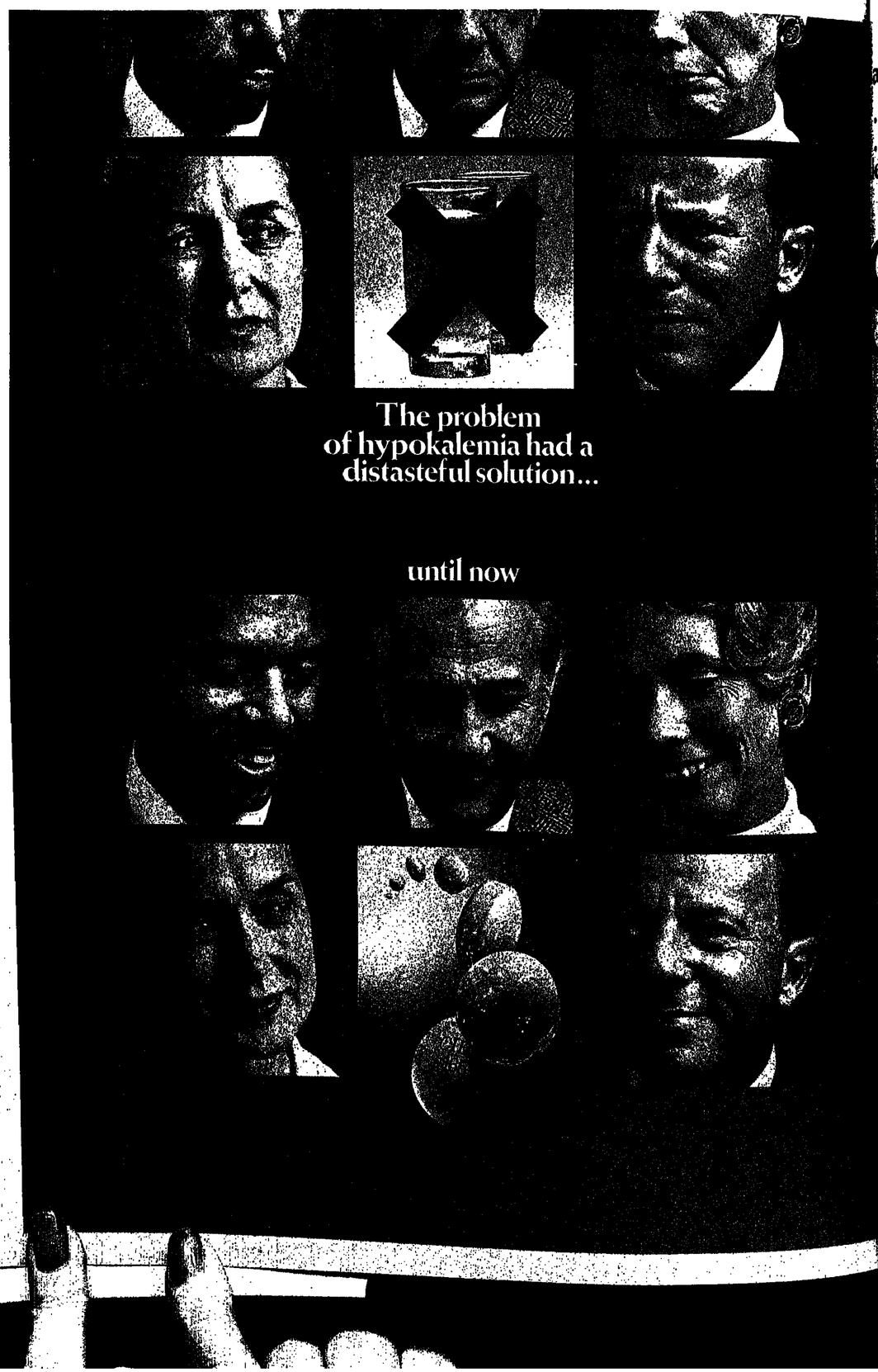
In the California trial, the laser has effectively controlled acute upper GI bleeding in two patients, one with hemorrhagic gastritis and the other with gastric ulceration, according to Dr. Richard M. Dwyer.

"This form of therapy," the investigator said, "has the potential of converting emergency surgery for acute upper GI bleeding into a relatively elective procedure and may offer an alternative mode of therapy for lesions not readily amenable to surgery."

Dr. Waitman, in summing up the results of the international trials to date, cautioned against premature enthusiasm or widespread adoption of the procedure by inexperienced endoscopists. The early findings are, however, sufficiently encouraging, he declared, to warrant "large well-controlled trials to determine the exact role of endoscopic laser phototherapy in the medical armamentarium."

Medical Meeting Schedule

June 26-27	*American Association for the Study of Headache, Dallas, Tex.*
June 26–July 1	*American Medical Association, Dallas, Tex.*
June 27–July 2	*Health Physics Society, San Francisco, Calif.*
June 27-30	*American Chinese Medical Society, Dallas, Tex.*
June 27-30	*American College of Preventive Medicine, Dallas, Tex.*
June 27-30	*American Medical Association Auxiliary, Dallas, Tex.*
June 27–July 2	*Radiation Research Society, San Francisco, Calif.*
June 28	*American Physicians Fellowship, Dallas, Tex.*
June 28–July 4	*International College of Surgeons, Cherry Hill, Pa.*



The problem of hypokalemia had a distasteful solution...

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Slow-K®
(potassium chloride)
low-release tablets 8mEq

e mission: to deliver K ients can take

The Slow-K wax matrix is nded to provide a controlled se of potassium to minimize likelihood of high local con- ations of potassium within the intestinal tract.

Comparison studies[1-3] show -K to be far more palatable and enient than liquid KCl. Fur- Slow-K caused much less , heartburn and diarrhea rence of abdominal cramp- s comparable). Also, no evi- of GI bleeding was detected Slow-K was administered or 14 days to 30 male volun-

The mission: to deliver K patients will take

The problem of patient compliance posed by the unpleasant taste and aftertaste of liquid potassium supplements is not a factor one need be concerned with when prescribing sugar-coated Slow-K tablets. For when compared to liquid KCl preparations[1-3] or to a potassium gluconate elixir,[1,3] Slow-K proved far more palatable—as well as more convenient and more acceptable—to the great majority of patients.

The chloride anion

Slow-K provides the chloride anion which, combined with K®, is essential for restoring normal acid-base and potassium balance in patients with hypokalemic alkalosis.[6]

Dependable potassium supplementation

Slow-K maintained normal serum K levels as effectively as liquid KCl preparations[2,3] and as a potassium gluconate elixir,[3] according to open-label crossover studies.[2,3,5]

And Slow-K has over 10 years' worldwide clinical experience, with over 4 billion tablets dispensed.*

*Potassium chloride tablets have produced stenotic and/or ulcerative lesions of the small bowel and ileoileitis. Similar lesions have also been reported with liquid K supplements. A few cases associated with wax-matrix tablets have also been reported. The frequency of these lesions, however, is much less with wax-matrix tablets (less than 1 per 100,000 patient-years) than with enteric-coated KCl tablets (40-50 per 100,000 patient-years). Note: Solid forms of K supplements are contraindicated in any patient in whom there is cause for arrest or delay in tablet passage through the GI tract.

Medical Research Department, CIBA Clinical Company, Summit, New Jersey. Controlled-release potassium supplementation during therapy. *Curr Ther Res* 16:734-741, 1974.

Potassium supplementation during therapy. *Curr Ther Res* 17:555-563, 1975.

Cavalieri MB, Dukstein WG, Arnold JD. Incidence of gastrointestinal bleeding with slow-release potassium chloride tablets. *Curr Ther Res* 16:685-690, 1974.

JC. Clinical evaluation of a new potassium chloride supplement. *Pharmacol* 14:624-629, 1974.

JP, Berkman PM, Lawrenz DR, et al. role of chloride in the correction of alkalosis in men. *Am J Med* 38:172-

CONTRAINDICATIONS
In patients with hyperkalemia, since a further increase in serum potassium concentration in such patients can produce cardiac arrest. Hyperkalemia may complicate any of the following conditions: chronic renal failure, systemic acidosis such as diabetic acidosis, acute dehydration, extensive tissue breakdown as in severe burns, adrenal insufficiency, or the administration of a potassium-sparing diuretic (eg, spironolactone, triamterene).
Wax-matrix potassium chloride preparations have produced esophageal ulceration in certain cardiac patients with esophageal compression due to enlarged left atrium.
All solid dosage forms of potassium supplements are contraindicated in any patient in whom there is cause for arrest or delay in tablet passage through the G.I. tract. In these instances, potassium supplementation should be with a liquid preparation.

WARNINGS
In patients with impaired mechanisms for excreting potassium, administration of potassium salts can produce hyperkalemia and cardiac arrest. This occurs most commonly in patients given potassium intravenously but may also occur when given orally. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic. Use of potassium salts in patients with chronic renal disease, or any other condition which impairs potassium excretion, requires particularly careful monitoring of the serum potassium concentration and appropriate dosage adjustment.
Hyperkalemia should not be treated by the concomitant administration of potassium salts and a potassium-sparing diuretic (eg, spironolactone or triamterene), since the simultaneous administration of these agents can produce severe hyperkalemia.

Potassium chloride tablets have produced stenotic and/or ulcerative lesions of the small bowel and ileoileitis. These lesions are caused by a high localized concentration of potassium ion in the region of a rapidly dissolving tablet, which injures the bowel wall and thereby produces obstruction, hemorrhage, or perforation. Slow-K is a wax-matrix tablet formulated to provide a controlled rate of release of potassium chloride and thus to minimize the possibility of a high local concentration of potassium ion near the bowel wall. While the reported frequency of small bowel lesions is much less with wax-matrix tablets (less than one per 100,000 patient-years) than with enteric-coated potassium chloride tablets (40-50 per 100,000 patient-years), a few cases associated with wax-matrix tablets have been reported. These data are from foreign marketing experience. Slow-K should be discontinued immediately and the possibility of bowel obstruction or perforation considered if severe vomiting, abdominal pain, distention, or gastrointestinal bleeding occurs.
Hypokalemia in patients with metabolic acidosis should be treated with an alkalinizing potassium salt such as potassium bicarbonate, potassium citrate, or potassium acetate.

PRECAUTIONS
Potassium depletion is ordinarily diagnosed by demonstrating hypokalemia in a patient with a clinical history suggesting some cause for potassium depletion. In interpreting the serum potassium level, the physician should bear in mind that acute alkalosis *per se* can produce hypokalemia in the absence of a deficit in total body potassium, while acute acidosis *per se* can increase the serum potassium concentration into the normal range even in the presence of a reduced total body potassium.
Treatment of potassium depletion, particularly in presence of cardiac disease, renal disease, or acidosis, requires careful attention to acid-base balance and appropriate monitoring of serum electrolytes, electrocardiogram, and clinical status of patient.

ADVERSE REACTIONS
Most common to oral potassium salts: nausea, vomiting, abdominal discomfort, and diarrhea. These symptoms are due to irritation of the gastrointestinal tract and are best managed by diluting the preparation further, taking the dose with meals, or reducing the dose.
Most severe adverse effects: hyperkalemia and gastrointestinal obstruction, bleeding, or perforation.

DOSAGE AND ADMINISTRATION
Usual dietary intake of potassium by the average adult is 40 to 80 mEq per day. Potassium depletion sufficient to cause hypokalemia usually requires loss of 200 or more mEq of potassium from the total body store.
Dosage must be adjusted to the individual needs of each patient but is typically in the range of 20 mEq per day for prevention of hypokalemia to 40-100 mEq per day or more for treatment of potassium depletion.

HOW SUPPLIED
Tablets (pale orange, sugar-coated), each containing 600 mg (8 mEq) potassium chloride; bottles of 100 and 1000.

Consult complete literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

3/1997

CIBA

from Britain

Vaccine Offers Rapid Pseudomonas Control In Severe Burns

Continued from page 26

with the University of Birmingham, we have worked out a computer programme which will identify some 50-odd changes and will classify them. We are now ready for a full scale clinical trial."

The first major trial will be in India, where *Pseudomonas* infection rates are high, facilities for treatment are more limited and the cost of antibiotics is very high. Many of the doctors taking part have worked at Birmingham.

"In our burns unit *Pseudomonas* is not a big clinical problem. If you take considerable trouble in prophylaxis using silver compounds, for instance you can prevent serious infection. It is, nevertheless, very common elsewhere, especially in underdeveloped countries."

DR. JONES

Vaccines against *Pseudomonas* are also under development in America. However, Dr. Bull said: "With theirs you have to wait 10 days or so before the vaccine reaches maximum effectiveness. This might well be too late as you don't have the opportunity to vaccinate everybody before they injure themselves."

Dr. Bull said that antibiotics are largely ineffectual against the hospital-borne infection. "There are one or two strains that are specially sensitive but they soon develop a resistance so you soon run out of antibiotic alternatives.

"We have tried sulphamylon, which many Americans prefer, but we do not like it so well. We have preferred silver nitrate as an alternative."

The Birmingham Unit is also experimenting with the use of pig skin, first developed in America several years ago, and certain plastics that have a moderate permeability to water vapour in burns.

Dr. Bull pointed out that exposure of burn tissue has some advantages but the major disadvantage is drying out tissue "that has been knocked out but not necessarily killed. We try and maintain a normal humidity to allow the cells to do the best they can in the way of survival. Perhaps a graft will be needed later."

Dr. Bull said the unit is experimenting with a technique, introduced in Yugoslavia, in treating fresh moderate thickness burns by tangential excision of layers of superficial tissues until a layer is reached that shows punctate bleeding. This tissue normally would be thought to be dead, for example, in vitro, it shows no respiration.

But "if you graft on top of that, then these burns do well and produce less scarring than if the full traditional excising had taken place," he added.

Still Looking

"We are still looking into how it is that tissue that is apparently dead, and that would certainly have died if the burn had been exposed, can be brought back into the body and incorporated under these circumstances."

Meanwhile, Dr. Roy Oliver and his colleagues, from the Department of Biological Sciences at Dundee University and at Ecotech Systems (UK) Ltd., are studying the use of collagen grafts in place of skin grafts.

It is thought that it is the cellular components of skin which induce the rejection process.

The antigenicity of collagen is in dispute, but in their work the team at Dundee have found that collagen is not antigenic in its pure form.

The collagen is obtained by treating donor skin with trypsin which digests the rest of the skin structures leaving behind a sheet of collagen.

The collagen is obtained by grafting on to the raw wound forms the framework into which the recipient's cells can grow from beneath and from the periphery of the wound.

Experiments with Rats

Their experiments with rats have shown that grafts of collagen show no sign of rejection after a period of months whereas grafts of untreated skin have been rejected in two weeks.

Moreover, the scar produced by the collagen is aesthetically better than that produced by untreated skin.

Dr. Oliver thinks there may be some tie-up between the better scars produced by the tangential excision method and the use of collagen grafts. The "apparently dead" layer of dermis also contains collagen. In both cases the collagen probably acts as a good filler for a wound so that less skin contraction needs to take place during healing.

On Page 17

A special section for your patients edited by Dr. Louis Lasagna, which will help you build effective doctor-patient relationships by explaining.

THE GOOD DRUGS DO

Put these pages specially designed to be removed from Medical Tribune, in your waiting room.

from Japan

Neurosurgeon Sees Precocious Puberty In 5-Year-Old Girl

Continued from page 26

sembling the mammary gland was palpable with tenderness. There were no lactation and development or pubic or axillary hair, nor was there premature onset of menarche.

In a general hematologic examination, erythrocytes counted 3,320,000; hematocrit was 26.9%, and the white blood cell count was 7,500. Other measurements included 6.4 gm/dl. of serum protein, SGOT 23, SGPT 8, LDH 379, Na 146 mEq/l., K 4.5 mEq/l, Cl 112 mEq/l, along with 500 ml/day of urinary volume and 1.015 of urinary specific gravity. The cerebrospinal pressure read over 400 mm. Hg., initially, on ventricular puncture. The fluid being watery clear with 142 mg/dl. total protein and 70 mg/dl. sugar.

Endocrinological findings included urinary LH reading as high as 260 IU/day: in TSH test and LH-RH test, TSH was found responsive, while the others remained low in response, showing a general decline of anterior pituitary function. HCG in cerebrospinal fluid was over 2,000 ng/ml.

On Aug. 7, perforation was performed, and Dimer X ventriculography was carried out. A filling defect was noted anterio-inferiorly from the third ventricle, and clear visualization of pineal depressions was obtained. On Aug. 9, 1975, V-P shunting was constructed; on Aug. 18, a partial excision of tumor was transventricularly carried out through right anterior craniotomy. Tumor was found to be reddish brown with partial exposure into the Monro's foramen.

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from Germany

New Test Eases Study Of Intermittent Acute Familial Porphyria

Continued from page 26

the harmful action of specific drugs, especially barbiturates, and in the case of women a warning is advisable regarding the risk of pregnancy. Such card is to be carried on the person against the possibility of an emergency.

Characteristics of acute intermittent porphyria were summarized as follows:

General Characteristics:

Genetically transmitted hepatic porphyria

Autosomal dominant heredity

Excessive excretion of δ-aminolevulinic acid and porphobilinogen in acute seizures

Clinical Signs of Acute Onset:

1. Sudden colic in abdominal region with constipation, flatulence and vomiting, without peritoneal muscular defense, without intestinal stiffening, and with further audible intestinal noises.
2. Reversible functional psychosis with depressive psychosis, intense retardation of psychomental reactions including clouding of consciousness, optical hallucinations, illusionary miscomprehension, disturbed orientation, spasms.
3. Porphyrin neuropathy with nonreversible motor peripheral disturbances in the distal muscle groups.

Seizure triggered by:

Barbiturates, sulfonamides, estrogens, pyrazolone derivatives, etc., or even by alcohol.

from France

Diuretics Useful in Congestive Heart Failure Therapy

Continued from page 26

present tendency towards hyperkalemia be dangerously increased. On the other hand, furosemide and ethacrynic acid are usually effective if used in very high doses (as much as 200 to 1000 mg of furosemide daily), said Professor Di Matteo.

Only a precise balance-sheet of the intake and output of water and salt should determine treatment under careful supervision. A constant and moderate supply of potassium chloride may be necessary in order to secure a sufficient renal output and not aggravate the renal insufficiency, he said.

Combining Therapy

If the congestive heart failure is mild or moderate, a daily prescription of thiazides and of potassium or even of the same thiazides combined with sparing diuretics is theoretically the best treatment. It is sometimes enough to give the diuretic two to four times a week. These prescription guidelines permit exceptions.

Ten per cent of the cases of congestive heart failure will not yield to routine treatment. The cause must be found: hyperthyroidism, cardiomyopathy, a dietary mistake, a secondary hyperaldosteronism.

Treatment by diuretics imposes constant supervision, with weight being checked several times a week and diuresis measured daily.

The clinical examination regularly assessing signs of congestive heart failure, will also seek the telltale signs of an overdose: asthenia, torpor, arterial hypotension, extracellular dehydration, said Professor Di Matteo. Blood and urinary electrolyte studies will aid in tracking down a hyponatremia, a hypokalemia, a hyperaldosteronism. Supervision also has a bearing on glycemia and uricemia.

Schizophrenia Increase

Medical Tribune Report

ROCHESTER, N.Y.—By 1985 there may be close to a million additional patients with schizophrenia in the U.S., according to Dr. Morton Kramer, of the National Institute of Mental Health.

Dr. Kramer told the Second Rochester International Conference on Schizophrenia, held here at the University of Rochester Medical Center, that his projection of statistical data concludes that by 1985 there will be an increase of approximately 30% or about 970,000 additional cases.

Doctors' Debate

MEDICAL TRIBUNE frequently receives extensive and well-documented communications from physicians on current subjects of controversy or those of great current medical interest. We welcome contributions in these areas for presentation in this new feature.

UGDP Computer vs. Clinical Data

WAS WITH GREAT DISTRESS that I read the remarks by Dr. Alvan R. Feinstein, Professor of Medicine and Epidemiology at Yale University who criticized the University Group Diabetes Program (MT, Mar. 10).

I had to write at length to other people who have apparently considered most us to be idiots who were involved the U.G.D.P.

As a clinic physician throughout the program, I take exception to the arguments of Dr. Feinstein as follows:

(a) He states that we "placed approximately half of the patients on a fixed dose of hypoglycemic medication in violation of all good clinical practice in diabetology." He is quite right that a fixed dosage was used, but this was, as I understood it at the time, because it was difficult to have from a statistical standpoint, many different patients on varying dosages of hypoglycemic agents and placebo. As you know, the medication was to be (for the AB program) (tolbutamide—tolbutamide placebo) three tablets.

Actually this is not too far off from an average dosage, and really is the maximum I personally have used in using oral agents. When I get above three tablets then I usually switch to one of the more potent agents such as chlorpropamide or tolazamide. One reason that I do this is that when you get above three tablets the cost of medication is so high as to be impractical.

Information Obtained

(b) We "failed to obtain, or accepted grossly defective, data for some 15 items of information basic to an adequate history of a diabetic, such as prior myocardial infarction, congestive heart failure or stroke, diabetic retinopathy, or peripheral vascular disease."

All this information certainly was obtained, at least on all the patients who entered the diabetes program at the Medical College of Alabama. We certainly did get people in who had the above problems and the reason was that the very nature of the protocol was made that only old patients were candidates and these were more likely to have complications; that is, only the heroses resistant patient could be used in the study.

It was required also that in accepting a patient it would be expected that he would live a certain period of time, and not being omniscient, mistakes were made in the selection of patients. As a matter of fact, one of the patients I personally selected was a black man who had a carcinoma of the lung and died a year or so after being in the program. Dr. Feinstein, I assume, being from Boston is able to commune with God, and able to select patients more carefully.

(c) We "ignored such goals of diabetic therapy as reduction of infection." This is a patiently ridiculous statement and I don't know where he got his information. Any patients who had infections were treated as indicated and I consider this particular argument to be so stupid as to require no further comment.

(d) We "neglected questions of comorbidity." I am not quite sure what he means here, but there is no question that the patients who were selected for the program had the co-problems of obesity and high blood pressure. In the Alabama clinic the patient were, for the most part, black patients, and as I recall, contained a rather large number of black females who tended to have high blood pressure and to be over weight. This was not a question of particular selection of patients other than by chance using a clinic population.

(e) We "performed glucose tolerance tests 'incorrectly' in four of 12 clinics, and kept 69 patients in the study although they did not have diabetes on the basis of GTT findings." To be in the study program a patient had to have a total of 500 mg. of fasting, one, two and three hour blood sugars added together. This may not have been the best criterion of diabetes, but this was chosen, and I assume for simplicity. Early in the program, I think that the Somogyi-Nelson, which used whole blood, was selected by some of the study clinics, whereas later the clinics began using the automatic machines which use serum or plasma rather than whole blood and I suppose this could have accounted for some unusual findings.

In answer to Dr. Feinstein's question about board certification, it just so happens that the particular correspondent here is board certified in internal medicine, graduated near the top of his class and was a member of Alpha Omega Alpha while in medical school. I admit that the program was not perfect in its conception, but that the best was done that could be done with the knowledge that we had at hand. The program was modified for the study of various factors as it proceeded, as any program worth its salt would be.

Composite Picture

I don't know Dr. Feinstein at all, don't know his background, don't know his reputation and I wonder if he has ever practiced medicine at all. Actually the patients we saw were probably a fairly accurate composite of what the average physician sees. The control that was achieved and the weight reduction achieved during the study were I suspect at least in the patients on the ad lib insulin program, pretty much approximated what the usual general practitioner sees and accomplishes in his practice.

I personally would have shot for higher goals, but it was decided that too many variables added into the program would cause statistical problems which were difficult to overcome with statistical methods available. I make no claim to be a statistician, but only claim to be clinician and I am growing increasingly weary of the sniping by individuals with preconceived notions about the proper treatment of diabetes mellitus. Because we have upset some ideas and some conceptions is good; at least we are making people think about the problem a little bit.

ARTHUR L. ENNIS, M.D.
Gadsden, Ala.

LET ME FIRST ASSURE YOUR READERS that I had nothing to do with the headline and first paragraph in your report of my comments about the UGDP study (MT, Mar. 10). The implication was that the UGDP investigators had "altered" and "falsified" their data with the deliberate intent to deceive. I did not make such an implication and I regret its occurrence in your report.

The letter from Dr. Ennis, however, provides excellent confirmation of the way in which the UGDP's clinical practice was inadvertently distorted for the sake of statistical doctrines and computerized processing. Dr. Ennis describes some of the many basic clinical strategies and data that were either changed to conform with "a statistical standpoint" or omitted because "too many variables . . . would cause statistical problems. . . ."

Major Disparity

The most striking feature of Dr. Ennis' comments is his clear demonstration that the UGDP's clinicians were (and apparently still are) unaware of the major disparity between what the clinicians observed and what was sent to the computer for analysis. Dr. Ennis says that the UGDP's clinicians did take adequate histories, did perform adequate physical examinations, did check co-morbidity, and did monitor infections. Since they were excellent clinicians—a point I have never questioned—I have no doubt that they did all these things.

An account of these clinical activities, however, was not allowed to become part of the research data collected for the UGDP's analysis. Dr. Ennis, despite his role as a "clinic physician throughout the program," seems oblivious of what was done to his clinical work when the UGDP's computerized data were assembled, analyzed, and published. I urge him to review the forms on which he and his colleagues transmitted their clinical observations to the UGDP's computerized media. Those forms—not the original patient records maintained by the clinicians—became the source of the UGDP's analyses and decisions. The forms contain no provision for the UGDP clinicians to record non-cardiovascular co-morbidity, infections, antecedent strokes, antecedent myocardial infarctions, severity of angina pectris, direct ophthalmoscopic examination, or many other crucial clinical phenomena.

I should also like to correct several other of Dr. Ennis' mistaken impressions. He disputes my comment about the UGDP's errors in glucose tolerance tests and in compliance with criteria for the diagnosis of diabetes mellitus. An account of the errors appears on page 759 of the UGDP's first main publication in *Diabetes* in 1970. Contrary to his statements, I am not now and have never been a Bostonian; I have been in the private as well as academic practice of medicine; and I

DR. FEINSTEIN

am a Fellow of the American College of Physicians.

Dr. Ennis also believes that my "sniping" at the UGDP study arises because I hold "preconceived notions about the proper treatment of diabetes mellitus". As I pointed out several years ago (*Clin. Pharmacol. Ther.* 12: 167, 1971), I believe that oral hypoglycemic agents have been over-used and I suspect that I would probably have treated most of the UGDP patients with diet alone. I do, however, hold the preconceived notion that a clinical trial should be a *clinical* trial.

Dr. Ennis has eloquently helped prove my point that the careful clinical practices of the participating investigators were ignored or transmogrified when the UGDP's statistical exercise was designed, carried out, analyzed, and biometrically reviewed. My comments about a poor quality of medical practice were directed not at the practical efforts of the UGDP's clinicians, but at what was done for the UGDP's computerized statistics. If Dr. Ennis is outraged by the way in which his own excellent clinical work was misrepresented in the UGDP's research data, he should address his complaint to the people who created the misrepresentations.

The basic truths of the UGDP study will be found not in the guarded collections of computerized forms and tapes, but in the original patient records at the individual institutions where Dr. Ennis and his colleagues observed the realities that did not reach the computer.

ALVAN R. FEINSTEIN, M.D.
Yale University School of Medicine
New Haven, Conn.

Controlling Cerebral Palsy

Medical Tribune Report

AUGUSTA, GA.—Eight days after implantation of electrodes in the anterior cerebellum and a receiver under the skin covering the chest wall, electrical stimulation has enabled a young boy with previously uncontrollable cerebral palsy to perform motor functions in a more relaxed manner and with greater ease, according to Dr. M. B. Allen, of the Medical College of Georgia.

Extracorporeal O_2 Salvages Dying Infants

By HARRIET PAGE
Special Tribune Correspondent

SAN FRANCISCO—Extracorporeal membrane oxygenation (ECMO) has been used to salvage four of eight infants and neonates who were near death from pulmonary or cardiac insufficiency, an Irvine, California surgeon reported here.

Speaking at the meeting of the American Society for Artificial Internal Organs, Dr. Robert H. Bartlett said he thinks "we may very well have something to offer these infants" with that approach.

Five neonates weighing 1.8 to 3.5 kg and three infants weighing 6 to 12 kg were treated. All were started on ECMO only after physicians concluded that their situation was irreversible, Dr. Bartlett said. "Case selection," he added, "was based on the best clinical guess that the infants would not survive."

Two Had RDS

Two of the newborns treated were suffering from respiratory distress syndrome. One of these survived. Two were suffering from meconium aspiration and one of these survived. The fifth neonate was suffering from persistent fetal circulation; this one survived.

One of the three infants treated suffered from postoperative low cardiac output; this infant survived. An infant with bacterial pneumonia died, as did one who was treated for drowning.

The babies were placed on venoarterial bypass for from one to 12 days, Dr. Bartlett said, with venous access through the right jugular or superior vena cava, and arterial access through the carotid or axillary artery to the atrium. Simple roller pump flow returned blood to the aortic arch at diastole, Dr. Bartlett said, with bypass flow rate maintained at 80% of normal cardiac output.

Heparin was used to keep whole blood clotting time at two times normal. In addition to oxygenation and perfusion support, ECHO allows extensive lung lavage and reduces trauma to the lung.

The lung disease babies who died showed total fibrosis at autopsy, Dr. Bartlett said, while the two-year-old drowning patient showed severe lung damage. The other fatalities demonstrated cerebral edema, he noted.

The four survivors, now followed for up to three years, show normal growth, psychomotor, and lung function, he added.

Trail Already Blazed

Dr. Bartlett, who performed the trials with Drs. M. Robin Jeffries, Nick Haiduc, and Alan B. Gazzaniga, all of the University of California, Irvine, said other clinicians had earlier "blazed the trail" for them. Successful perfusion for pulmonary insufficiency in an infant was reported from Quebec, and others had used membrane oxygenators in 1969, although none of these latter cases had been successful, he noted.

One Man... and Medicine

ARTHUR M. SACKLER, M.D.
International Publisher, Medical Tribune

Pity The Poor Pig

Swine Influenza or Hot Potato?
or
Which Little Pig Went to Market?

OUT WEL..

We know it's a serious matter. But, I'm damned if it's laughable.

As an avid reader of *Science* and a number of other "prestigious" publications, I must confess to a rather serious case of "influenza vertigo." At this point I don't know who's more to be pitied, the poor pigs (have their names been taken in vain?), or politicians, public health figures, and the public.

I'm beginning to wonder, perhaps we need an S.O.S.S. (Society on Swine Safety). Why? It's beginning to look as though we are going to have more of a fuss, more politicking and lobbying as to whether swine should be vaccinated than on the decision to inoculate 200 million Americans against swine influenza.

Science (May 28, 1976) reports workshops and meetings being held in Bethesda, Md., by the Bureau of Biologics, in Hyattsville, Md., by the Department of Agriculture's Animal and Plant Health Inspection Service, and of course a meeting of international experts has been convened by WHO. As to the subject of their meetings, frankly I am getting a bit confused. I don't know, at this point, whether it is related to Swine Influenza, the "New Jersey Flu" or the "Fort Dix Disease."

Who's Disease?

I can't help remembering the attributions in the medical literature as to the nomenclature of the disease produced by that tortuous little organism technically termed Treponema pullidum or Spirochaeta pullida. The French called it the Italian disease; the Italians called it the French disease. There was even an attempt made by Europeans generally to palm it off on the American Indian. And so it went.

We now face a new international cause celebré. A statement issued by the National Live Stock and Meat Board, an organization financed by farmers and packing houses, put it this way: "There's much more conclusive evidence of transmission of influenza from humans to hogs than vice versa."

Science went on to comment on the "touchiness of the industry" and we note their suggestion that "the industry" objects to the character slaughter of their hallowed hogs. The growers have a point when they hold that the strain found at Fort Dix should be called "New Jersey Flu" in accord with the tradition of geographic identification of the Hong Kong or Asian flu. We expect to hear shortly from New Jersey's Chamber of Commerce objecting to that diagnostic stigma. The problem arises whether the terminology of "Fort Dix Disease" would not in turn bring forth the righteous protests of the Department of Defense.

The situation is really quite serious. No one yet has had the temerity to identify himself with the proposal that we inoculate 70 or 80 million pigs annually and even the man to whom such an idea was attributed has called it "a bunch of poppycock." Nonetheless, the prospect has struck terror into the heart of the swine industry whose partisans believe that a national swine vaccination program would give pigs or hogs or swine an undeserved bad name. Anti-pig pejorative propaganda has a long and notorious background:

"And the swine . . . is unclean to you. Of their flesh shall ye not eat," *Leviticus* 11:7-8.

"For buying or selling of pig in a poke" originated in *Five Hundred Points of Good Husbandry*, 1557.

"You can't make a silk purse out of a sow's ear," said Jonathan Swift, *Polite Conversations, Dialogue* #2, 1738.

In Medicineland, U.S.A.

There are a few other facts which we cannot escape:

1. Swine Influenza does not kill pigs; "mortality is generally less than one percent." (*Science*, May 28, 1976)
2. "Typically, the pigs will cough, develop fevers, breathe with difficulty, fall prostrate, and appear to be on the verge of death." *(Ibid.)*
3. "After several days, they recover rapidly." *(Ibid.)*
4. "20 percent of young pigs and 40 percent of older pigs were found to have antibodies against swine flu." *(Ibid.)*
5. Government officials do not have data to "indicate whether a vaccination campaign would be cost-effective." *(Ibid.)*

However, one participant in a recent conference reported in *Science* suggested that "if the vaccination campaign is successful in humans, that will 'break the back of the epidemic,' thereby letting Agriculture off the hook." Another brilliant proposal maintained that a "search for swine flu elsewhere [would help] establish that the United States is not the bad boy in this and might help clear the name of the pig industry."

As to the marvels of Medicineland, U.S.A., please note the following anecdotal observation in *Science*:

"Shortly after the Fort Dix outbreak, a prominent flu investigator was blocked from examining swine herds around the base by New Jersey officials, who were reluctant to 'smear the swine population.' 'There was no way they could stand the political pressure,' said one veterinary expert." *(Ibid.)*

In brief, the whole situation has demonstrated a basic socio-political fact of life.

Is it possible in the United States to vaccinate 200 million humans in one fell swoop?

CAN DO!

Can we vaccinate 70 million American pigs against Swine Influenza?

Well now, let's not rush such things.

But lest one gets too cynical, may we report a research breakthrough on the transmission of Swine Influenza. The Fort Dix Swine Influenza strain is clearly infectious in pigs as demonstrated in an experiment, commented on in *Science*—"the strain found in recruits at Fort Dix readily infected five pigs, which in turn transmitted the disease by contact to five other pigs."

The one thing I didn't learn is:

"Which little pig went to market?"

Intermittent Heparin Found as Effective, More Convenient, Safer Than Continuous

Continued from page 1

in two patients on intermittent and three on continuous therapy.

"Serial values for clotting times, fibrinogen/fibrin degradation products, and soluble fibrin complexes were never statistically different in the two groups," the investigators noted.

Less Hematocrit Decrease

Another observation, however, indicated in their opinion that intermittent administration may have a safety advantage—patients given heparin by this method showed a lesser mean decrease in hematocrit than did those on continuous administration.

It is possible, they believe, that brief periodic respites from anticoagulation will allow microscopic fibrin deposition within platelet plugs to counteract small bleeding points but not allow major thrombosis. By contrast, continuous heparin provides no rest periods and thus "may promote continued occult blood loss from multiple small bleeding sites."

Citing some recognized drawbacks of continuous heparin administration, Drs. Bynum and Wilson pointed out that the use of an infusion pump increases expense, may disturb sleep, and makes ambulation difficult. Also, continuous administration calls for careful calculation and regulation of heparin dosage to insure proper dilution in intravenous solutions, and may require placement of indwelling catheters with added risk of infection.

"Therefore, in the absence of any demonstrable advantage to continuous infusion," they concluded, "considerations of convenience and safety make intermittent heparin the method of choice in the treatment of pulmonary embolism."

Tribune Economic Analysis

Market Jittery As Dow Hovers Around 1000

BY ELIOT JANEWAY
Consulting Economist

Wall Street exuded confidence as long as business was unarguably bad; bad business pays a market dividend in the form of low interest rates. By the same token, a business improvement taxes the market with the burden of rising interest rates.

In this atmosphere, the stock market is reversing its familiar pattern of recent months. The domestic institutions have been trying to push the market over 1,000 in order to take profits; the foreign institutions have been buying over 1,000, and the retail public has been selling at 1,000.

This neat division of labor is no longer working out. The domestic institutions have been outgunned by the retail public, whose selling has discouraged them from buying. The foreign institutions, meanwhile, have been thrown off balance by the failure of the market to follow through on its "up" days. They have stopped supporting the market on its "down" days. Now the domestic and foreign institutions are on the sidelines.

Every time the Dow gets above 1,000, the public checks out. In the past, market tops above 1,000 followed by sell-offs below it would have rekindled shopping for bargains. This time, however, weakness under 1,000 is accelerating the public's drive to get out of stocks and into cash.

Each bounce over 1,000 makes the market riskier; every bounce under 1,000 opens the shopping bag for bargains. For the time being, it's an oscillating market.

Ask Janeway

Twenty years ago, our family mine brought in $25,000 in royalties over a two-year period. We had no way of knowing how much money we would receive at any one time, or how long the royalties would continue. Not knowing how to handle our money, we lost most of it. Now the royalties are coming in again, and we do not want to make the same mistake. We have begun investing in a liquid asset fund. Is this a safe investment?

Ohio Physician

Liquid asset funds are perfectly safe, but they are not investment vehicles. They are a device for holding liquidity in reserve while waiting for an opportunity to invest it. They are most attractive, however, when interest rates are high.

Before you invest, check whether your royalty income is entitled to any tax deductibility. Then write me again about your investment availability.

Send your questions on finances, investments, taxes to Janeway, MEDICAL TRIBUNE, *880 Third Avenue, New York, N.Y. 10022.*

IMMATERIA MEDICA

The End of Civilization As We Know It

Reports from many parts of the country indicate that short hair is coming back—at least for men. In San Francisco, *the* bastion of the shaggy look, barbershops report business is up 30%. In Boston a "barber's college," as we used to call them, reports enrollment is up 20%. Barbering jobs are going begging. Nobody's around to harvest the hair.

Some barbershops are trying to train their customers to come in every two weeks which is quite a difference from every two years. We may have to ride this wing of the pendulum all the way back to Old Baldie, once the summer standard for young boys.

We'll certainly be sorry to see the shaggy heads go, even if it helps to tell men from women.

It's our hope that wigs will stay. We have been pro-wig for a long time, not just because our forefathers wore them, but because you can enjoy them without wearing them. A man whom we will identify only as J.A. has had more fun with a wig than anyone with hair—a lot of hairy fun, that is.

J. A. is a member of the board of several major industrial companies—and he's completely bald. But he believes that life, like art, is not as bad as it's painted, especially by some of his fellow board members.

One day he bought a shoulder-length wig and, donning it, sallied into the board meeting, shaking hands with everyone and being his usual jolly self. Half of them had a hard time recognizing him—and the other half was startled into shocked silence. He argued various issues with more vigor than usual, swinging and swirling his head to show off his shoulder length curls to their best advantage. His fellow board members were too embarrassed and perplexed by his new-found hair to say a word.

But after he had won his point, which was they had better catch up with the younger generation, he reached up and whipped it off, saying, "Boy, this is just too hot for me!" And stuffed it into his pocket.

There was about a 20-second double take—and then they all broke out laughing. As he tells it, "It's the first dividend, they've paid as human beings."

But if this is the end of the Age of Aquarius, we look forward to its revival, especially the music in *Hair*.

Clinical Cliché

The drainage was poor.